Socialisation and psychological wellbeing: Modelling the impact of the prenatal maternal social environment on offspring mental health outcomes in middle childhood

Eric Spikol

BSc. (Honours) Psychology

School of Psychology

Faculty of Life & Health Sciences

Ulster University

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Summary

It is well accepted that aspects of the prenatal environment can affect the foetal genome and offspring health/mental health outcomes. Previous research has described these effects manifesting as specific epigenetic adaptations to harsh/deficit environments that become maladaptive in a normative environment. It was hypothesised that the prenatal maternal social environment constituted a deficit environment for a mother in social isolation, that epigenetic adaptations would 'prime' the offspring genome with adaptations for survival in an isolation environment, that offspring primed for a specific social environment would suffer distress in a 'mismatched' environment, that offspring primed for social isolation would be more resilient to the effects of isolation than other children and, that this distress would manifest as psychopathology symptomology. Prenatal maternal and child data were sourced from the Avon Longitudinal Study of Parents and Children (ALSPAC, N=15,645) to test these hypotheses. The prenatal maternal social environment was modelled as 5-dimension construct with the maternal population comprised of 3 latent socialisation profiles: High, Baseline, and Low. The child social environment was modelled as a unidimensional construct of *Socialisation*, and psychopathology in middle childhood was longitudinally modelled as 4 distinct trajectories: High-Stable, High-Decreasing, Low-Stable, and Low-Increasing. Prenatal socialisation and child socialisation influenced the likelihood of psychopathology trajectory membership, indicating low distress for environmental match, high distress for mismatch, and a resilience effect in offspring primed for isolation. These results highlight the importance of socialisation during pregnancy for both mother and child and could lead to increased clinical/community awareness of prenatal isolation. Findings here re-contextualised psychopathology symptomology as partially environmentally dependent, suggesting a continuum of inborn adaptive/maladaptive behaviour which influenced psychopathology risk. Future work will focus on replication in other large populations, exploring this effect with specific disorders, and exploration using genomic data.

Abbreviations

χ^2	Chi square
5-HTT	Serotonin transporter protein
ACE	Adverse childhood event
ADD	Attention deficit disorder
ADHD	Attention deficit hyperactivity disorder
AIC	Akaike information criterion
ALSPAC	Avon Longitudinal Study of Parents and Children
ANOVA	Analysis of variance
BIC	Bayesian information criterion
CASCOT	Computer assisted structured coding tool
CCEI	Crown-Crisp Experiential Index
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CHES	Children and Health Education Study
CI	Confidence interval
CiF	Children in focus
CNS	Central nervous system
COCO90s	Children of the children of the 90s
COMT	Catechol-*O*-methyltransferase
COVID-19	Coronavirus disease 2019
CPTSD	Complex post-traumatic stress disorder
df	Degrees of freedom
DNA	Deoxyribonucleic acid
DOB	Date of birth
DSM-5	Diagnostic and Statistical Manual of Mental Disorders 5
EEG	Electroencephalogram
EFA	Exploratory factor analysis
ELSPAC	European Longitudinal Study of Parents and Children
EPI	Eysenck Personality Inventory
ESEM	Exploratory structural equation model
fMRI	Functional magnetic resonance imaging
GP	General practitioner
GWAS	Genome wide association study
HPA	Hypothalamic-pituitary-adrenal
HPG	Hypothalamic-pituitary-gonadal

ICD-10	International Classification of Diseases 10
IPSM	Interpersonal Sensitivity Measure
IQ	Intelligence quotient
IS	Interpersonal sensitivity
ISER	Institute for Social and Economic Research
LCA	Latent class analysis
LGM	Latent growth model
LGMM	Latent growth mixture model
LMR-LRT	Lo-Mendel-Rubin likelihood ratio test
LPA	Latent profile analysis
MAOA	Monoamine oxidase A
MHCH	Maternal high/child high
MHCL	Maternal high/child low
MHCM	Maternal high/child medium
MLCH	Maternal low/child high
MLCL	Maternal low/child low
MLCM	Maternal low/child medium
MMCH	Maternal medium/child high
MMCL	Maternal medium/child low
MMCM	Maternal medium/child medium
MPFC	Medial prefrontal cortex
MRC	Medical Research Council
MRI	Magnetic resonance imaging
NHS	National health service
NNFI	Non-normed fit index
NS-SEC	National statistics socio economic classification
OBGYN	Obstetric gynaecologist
OR	Odds ratio
PEARL	Project to enhance ALSPAC through record linkage
PET	Positron emission tomography
PS	Prenatal stress
PTSD	Post-traumatic stress disorder
RBM12	RNA-binding protein 12
RMSEA	Root mean square error of approximation
SD	Standard deviation
SDQ	Strengths and difficulties questionnaire
SES	Socioeconomic status

SLE	Stressful life event
SNP	Single nucleotide protein
SRMR	Standardised root mean square residual
SSABIC	Sample size adjusted Bayesian information criterion
TLI	Tucker-Lewis index
TMEM132D	Transmembrane protein 132D

Chapter 1

Main introduction

1.1. Introduction: Thesis Proposal

Decades of research have shown that factors in the prenatal maternal environment can influence health and mental health outcomes of the child via epigenetic modifications to the child's genome (Perera & Herbstman, 2011; Cortessis et al., 2012). These changes represent the interaction between genes and the environment and function as an adaptive mechanism to prepare the foetus for survival in a specific expected environment (Heijmans, Tobi, Lumey, & Slagboom, 2009). If a prenatal environment deficient in nutrition could produce physiological adaptations to famine (Heijmans et al., 2008), it followed that a prenatal environment deficient in social contact could potentially produce psychological adaptations to isolation. It was hypothesised that if a pregnant woman was in social isolation, her foetus' genome would undergo epigenetic modifications designed to 'prime' the child for survival in isolation, and if in social isolation later on in life, that child's mental health would fare better than a peer who was 'primed' for a social environment. Further, it was predicted that the child carrying a 'social phenotype' for isolation adaptation would be maladapted for a highly social environment to the detriment of their mental health. Lastly, it was hypothesised that this effect would be present even after controlling for the developmentally crucial postnatal environment.

This thesis aimed to explore these research questions by utilising prenatal and child data sourced from a large population longitudinal study, designing a methodology to generate a valid statistical framework for testing these proposals, and presenting the results here. This chapter will introduce the main theories and processes on which these hypotheses were based: the intersection of evolution and psychology, epigenetic processes, prenatal influences on mental health outcomes, and the social environment as a deficit environment capable of triggering epigenetic processes, as well as an overview of the empirical chapters, a justification of the relevance of this work, and the goals/aims of this thesis.

1.2. Evolutionary Influences on Psychology

Every human being is a product of all the environments which preceded them, going back to the beginning of life on Earth. Countless factors contributed to the advent of each person, themselves a factor in the contemporary environments of others and ultimately, every human being to follow. Many events shaped humanity's course over millions of years (Uyeda, Hanse, Arnold, & Pienaar, 2011), including several climate changes (Behrensmeyer, 2006; Stewart & Stringer, 2012), fluctuations in food type/availability (Rodríguez-Gómez, Rodríguez, Martín-González, Goikoetxea, & Mateos, 2013; Hardy, Brand-Miller, Brown, Thomas, & Copeland, 2015), and mass migrations (Timmermann & Friedrich, 2016). However, humans are the only animals to achieve 'post-evolutionary' status in adapting our environments to suit ourselves. This section will cover the relationship between human evolution and psychology, specifically a brief overview of evolutionary psychology and how evolutionary theory underlies the hypotheses this work explored.

Change in human brain physiology has remained relatively static and barring injury, deformation, or disease, the modern brain features the same structures and physiology as the brains of the first *Homo Sapiens sapiens* (Neubauer, Hublin, & Gunz, 2018). It is possible to see the likely life trajectories of ancestors in modern human development, from the physiological to the cultural. That they were socially cooperative was obvious, but there must also have been conflict between individuals and groups, fractious beliefs, and great innovation but also those resistant to change. It is not hard to imagine the petty concerns of a small modern neighbourhood playing out in a small Neolithic village, but contemporary humans certainly differ from these Stone Age ancestors. If the human brain has changed so little over 10,000 years, what explains the delta between us?

Evolutionary psychology applies an evolutionary perspective in exploring the factors which potentially shaped our modern minds. In viewing behaviour as a set of reactive adaptations, it establishes a cause-effect chronology of human psychological development seeking a unified theory to explain everything from mate selection (Barber, 1995; Caporael, 2001) to gendered behaviour (Luxen, 2010) to altruism

(Kruger, 2003; De Waal, 2008). The concept of universality is particularly important when discussing evolution as it is the hallmark of a species level adaptation (language use, cognitive development, etc.) over a localised trait (skin colour) or a cultural adaption (a specific language). Without universality, a given adaptation cannot be generalised to all humanity, a distinction important when discussing the species as a whole. Evolutionary psychologists posit that both conscious and unconscious behaviours are the result of adaptations to ensure the best chance at survival. For example, examining the role of perception physical appearance in mate selection from an evolutionary psychological perspective would be less about how the attractiveness of specific individuals and more about the influence of biological imperatives to select the mate whose offspring might be more fit and apt to survive (Puts, 2016). Taking this view, genes for successful behaviour persisted by natural and sexual selection, and psychological mechanisms that boosted ancient survival odds became a part of contemporary human psychology.

Modern humanity has laid a fair amount of psychological baggage at the feet of its ancestors. Societal problems are often blamed on the inherited 'primitive' survival-based psychologies of the past. For example, racism and xenophobia have been called a remnant of kin favouritism and tribalism, harkening back to an alleged time of resource scarcity and inter-group competition (Hammond & Axelrod, 2006; Jones, 2018). Contemporary conspiratorial ideation and anti-science beliefs are held up as examples of the human mind accepting simplicity over complexity in problem solving (Abalakina-Paap, Stephan, Craig, & Gregory, 1999). Acting simply and quickly was advantageous in the presence of predators but few modern problems are as simplistic as a tiger in the bushes. Such notions highlight how evolutionary principles can guide how the general public and the field think about psychology by relating the present to the primitive. However, influences on individual behaviour are multifactorial and a purely evolutionary outlook can miss contextual environmental factors, including lived experience and societal/cultural influences (Benton, 2000). Without early humans to gather data from and lacking written accounts of their thoughts, emotions, and behaviours, many evolutionary psychology theories could be called speculatory in nature (Siegert & Ward, 2002).

While there are several valid criticisms of evolutionary psychology, the evolutionary process was paramount in creating the species humanity is today, with human intellectual ability enabling everything from agriculture to written language to advanced technology. Evolution moves at a glacial pace, meaning that if major adaptations were the result of major environmental pressures, a mechanism must have existed for minor adaptations to short-term environmental pressures or humanity would not have survived. Environmental pressures interact with the genome, resulting in different genes being switched on or off by chemical processes (Guerrero-Bosagna & Skinner, 2012), changing expression of the genes rather than rewriting the genome itself. This mechanism, epigenetics, functions throughout the lifespan but also can occur *in utero*, allowing the prenatal environment to affect the foetal genome.

This science lay at the centre of this thesis' hypotheses: could a short-term prenatal environment force an adaptation affecting offspring behaviour and mental health? A large body of literature exists on physical health outcomes due to the prenatal environment but very little on the relationship between it and mental health outcomes/psychopathology. Proposed here was that the evolutionary survival drive was an overarching process with epigenetic mechanisms functioning as short-term adaptations to a social environment, and that those adaptations would become maladaptive if the environment did not persist, with psychopathology an expression of the distress of this environmental 'mismatch'. This premise conceptualised psychopathology as the product of multiple risk factors, with the distress of social environmental mismatch predicted to increase that risk.

Evolutionary theory was central to this thesis, but this work should not be considered a work of evolutionary psychology, primarily because it did not follow the core principles and premises of the domain (Buss, 2015). Rather, this thesis sought a broad evolutionary approach by viewing survival drive as a proximal influence on the genome but a distal influence on the individual, with the most important factor being the child's eventual environment and if it differed from the 'expected' prenatal environment. Like evolutionary processes, epigenetic processes are also driven by immediate survival to bolster the odds of eventual reproduction, but due to gene x environment interactions, the impact on the individual is

immediate, rather than the product of hundreds of thousands of years. This broad approach was adopted to incorporate overarching evolutionary theory, epigenetic processes, environmental influences, psychosocial, and socioeconomic covariates into a model testing the impact of the prenatal environment on child psychopathology.

These epigenetic processes can be viewed as the 'middle-man' between evolutionary theory and effects on the individual during their lifespan. Mechanisms of micro-adaptation have potentially governing interactions between the human genome and short-term environments for the entirety of human existence, with the research of the past several decades beginning to expose their methods.

1.3. An Introduction to Epigenetic Theory

Environmental pressures can affect the genome on both the population and individual levels. Where the evolutionary process functions in the extreme macrocosm, slowly producing adaptations to systemic environmental pressure, epigenetics functions in the microcosm of the individual, quickly adapting to the immediate environment. This is a process of localised, generational 'micro-evolution'; fine-tuning of the genome by switching genes on/off without altering their sequence, triggered by environmental interaction (Mattick, Amaral, Dinger, Mercer, & Mehler, 2009). A change occurs either by the addition of a methyl group to a DNA segment (known as 'methylation', preventing transcription) or by the methyl group attaching to a specific histone (histone modification, changing how the sequence is read). These modifications can be expressed within the lifespan (Khanherkar, Bhatia-Dey, & Csoka, 2014) and are heritable (Carey, 2012; Low, Gluckman, & Hanson, 2012; Yehuda et al., 2016). The epigenetic mechanism allows individuals to adapt to short-term environmental changes in more discreet ways compared to species-wide, major evolutionary adaptations. Here, a 'short-term' change may still span decades (famine, drought) or even centuries (climate shifts, coastal geographic changes) but pales in comparison to the approximate 1 million years a major evolutionary shift takes (Klein, 1995; Uyeda, Hansen, Arnold, Pienaar, 2011).

Epigenetic modifications function towards individual fitness rather than population fitness and can be viewed as a risk/reward system. If a pregnant woman is under-nourished, an epigenetic adaptation sacrificing birth weight for accelerated post-natal development is risking survival on the possibility of increased nutrition after birth. Low birth weight is an immediate adaptive response (IAR) to deficit, but the accelerated post-natal growth represents a predictive adaptive response (PAR), assuming the child will persist in a deficit environment and need to conserve/consume additional nourishment (Gluckman, Hanson, & Low, 2019). Both responses can be beneficial by increasing survival chances for the child but can paradoxically lead to negative health outcomes. Low birth weight is associated with many health issues (McCormick, 1992; Hack, Klein, & Taylor, 1995) but especially cardiovascular disease and mortality (Barker, 1997; Gluckman, Hanson, Buklijas, Low, & Beedle, 2009), while deprivation-driven accelerated post-natal growth is associated with increased risk of obesity (Ravelli, Stein, & Susser, 1976) and hypertension in middle age (Stein, Zybert, van der Pal-de Bruin, & Lumey, 2006).

These epigenetic changes can be understood as priming for an expected severe environment via a series of cost-benefit 'decisions'. The thrifty phenotype hypothesis (Hales & Barker, 1992) explains this as preserving survival at all costs with the expectation of reproduction happening before poor health outcomes manifest. Prioritising brain and lung development over foetal birth weight in a malnourishment situation is a prime example, 'gambling' on the infant being able to catch up in growth development after birth, despite the previously discussed long-term health outcomes of low birth weight. In addition, modifications with expressed consequences are preferable to the damage of developmental disruption from a biology viewpoint (Gluckman, Hanson, & Low, 2019). That humans seek to survive past the reproductive age out of an enjoyment of life and a desire to continue living is immaterial. All of hominid evolution took place prior to agrarian settling (Tooby & Cosmides, 1990, as cited in Gluckman, Cutfield, Hofman, & Hanson, 2005) and in the intervening 12,000 years, humanity has sidestepped many evolutionary concerns. Species survival no longer depends on every available human reproducing. Our consciousness of the nature of death has meant survival is now for survival's sake; a population wanting to exist as long as possible purely for the experience of

existing. Humans are also complex organisms with a long maturation period compared to non-primate mammals, and while humanity's advancement as a species is impressive, all of human history is considered a novel environment in evolutionary terms (Gluckman, Cutfield, Hofman, & Hanson, 2005).

Epigenetic processes are not limited to the maternal environment influencing a foetus *in utero*. Modifications to the paternal genome based on the father's various lived environments can be incorporated into the foetal genome at conception (Chong et al., 2007; Rando, 2012; Soubry, 2015). These changes can be passed down through both lines of inheritance in a very illuminating example of how complex and mutable both the human and individual genomes really are. Paternal epigenetic influence on behaviour has been found in animals (Franklin & Mansuy, 2010; Klengel, Dias, & Ressler, 2016) and in humans (Soubry, Hoyo, Jirtle, & Murphy, 2014).

Having established the processes which govern short-term adaptations and the mechanisms by which these takes place, attention must be paid to the outcomes of gene expression risk. Generally, 'adaptive' behaviour is that which fits/is appropriate to a given environment where 'maladaptive' indicates problematic behaviour, usually in a survival context. The extinct dodo bird is a perfect example as its island environment featured abundant food and lacked natural predators. Without defence mechanisms, it was easy prey for the humans who discovered it and the invasive species they brought, leading to its extinction (Cheke, 2014). Behaviour that was advantageous in one environment, environmental fit, became a liability when the environment changed, leading to environmental mismatch (Godfrey, Lillycrop, Burdge, Gluckman, & Hanson, 2007; Li, van Vugt, & Colarelli, 2017). In the above example, the child *in utero* during famine was epigenetically primed for a severe environment, one where rapid postnatal growth and continued economy of calories would be vital for survival. However, if the child were to be born into and grow up in a normative environment, the phenotypic expressions would become maladaptive and would result in adverse health outcomes.

The past several decades have seen a sharp increase in studies devoted to epigenetic effects in humans, from general disease epigenetics (Rodenhiser, 2006;

Feinberg, 2007) to specific pathology, including cancer research (Feinberg & Tycko, 2004; Howell, Liu, Ren, Behlen, Fodstad, & Riker, 2009; Sharma, Kelly, & Jones, 2009). Exploring the role of phenotypic expression in disease also delves into the complicated relationship between humans and their environments. The idea that one's genome was set in stone from conception, that DNA was the unchanging blueprint of the individual, has shifted to a more interactional model (Dolinoy, Weidman, & Jirtle, 2007; Liu, Li, & Tollefsbol, 2008). It is understood that epigenetic modifications have physiological implications but given that the human brain is a physical organ and that phenotypic expression influences brain development, it is logical to conclude such modifications could affect the brain and by extension, individual thoughts, attitudes, and behaviours. Exploring the psychological impact of epigenetic expression is also a growing field seeking to understand how environmental pressures, even those experienced *in urtero*, could factor into an individual's psychology or even psychopathology, later on in life. A full exploration of prenatal epigenetics in humans features in Chapter 3.

1.4. Prenatal Stress and the Prenatal Environmental Adaptation Hypothesis

Frequently conceptualised as a single semi-permeable system, the human body is better described as a macrosystem hosting countless microsystems, the interactions of which are only recently being fully understood (Adomian, Adomian, & Bellman, 1984; Wilder, 1995). The physiological interplay between the mother's body and its dependent, from embryo to foetus to infant, is also a complex series of systems with the placenta and umbilical cord serving as the connection points. The placenta provides access to oxygen and nutrition from the mother's blood, serves as waste disposal for the foetus, is a base of pregnancy hormone production/regulation, and acts as a barrier against infection (Mayo Clinic, 2020). Many types of chemical compounds can pass through the placental barrier, including drugs and maternal hormones (Haig, 1996; Griffiths & Campbell, 2015). These hormones function as chemical signals, informing of everything from the mother's mood (Monk, Fifer, Myers, Sloan, Trien, & Hurtado, 2000) to the environmental pressures discussed above. Hormonal communication is not the only connection between the foetus and

the rest of the world, as they are also responsive to sound and touch, but it is the main venue by which the maternal environment affects the foetus.

Environmental pressures (and individual pressures) are experienced by the mother as stress which is very easily communicated to the foetus. Cortisol, 'the stress hormone', is a glucocorticoid largely responsible for several physiological responses to stressors and is one of the hormones able to cross the placental barrier. As lack of nourishment or presence of infection can result in an epigenetic effect (Barker, 1997; Heijmans et al., 2008; Kundakovic & Jaric, 2017), so too can environmental stressors though the release and uptake of cortisol. However, environmental influences *in utero* should not be thought of solely in terms of disaster or deficit, as they are part of regular development in many species. For example, depending on the season (autumn or spring) the meadow vole foetus grows a heavy or light coat of fur pre-birth to be adapted to the coming winter or summer (Gluckman, Hanson, & Low, 2019). Positive information is also communicated to the foetus via the mother's biochemistry and studies have shown that maternal meditation and mindfulness practices during pregnancy had beneficial infant health outcomes (Vieten & Astin, 2008; Chan, 2014).

Studies into prenatal maternal stress have increased over the past several decades along two distinct paths: non-human experimental design studies and human retrospective or prospective opportunistic studies. The main obvious difference is the specific population, as ethics would preclude deliberately stressing pregnant women to cause possibly detrimental effects to their offspring. Non-human mammal studies abide by ethical standards for animal experimentation and are able to incorporate more theory into experimental design, including focusing on domain-specific adaptations. Hayashi, Nagaoka, Yamada, Ichitani, Miake, and Okado (1998) found that stressors including overcrowding affected the development of spatial abilities in the offspring of exposed rats. Investigating spatial memory and anxiety, Schulz et al. (2011) found a gender effect in the offspring of prenatally stressed rats; spatial memory issues in males and increased anxiety in females (for spatial memory effects in humans, see Plamondon et al., 2015). Unpredictable noise stressors on pregnant Rhesus monkeys (Clarke, Wittwer, Abbott, & Schneider, 1994) and pregnant rats (Mastorci et al., 2009) produced increased cortisol responses in offspring, while

noise/light stressors in expectant rats produced heightened open space anxiety in offspring (Weinstock, Matlina, Maor, Rosen, & McEwen, 1992).

In a review of both human and animal studies, Beydoun and Saftlas (2008) discuss the parallels of this research, noting that physiological effects occur in both and that psychological effects in animal models mirror results in human samples. Kingston, Tough, and Whitfield's (2012) review of human studies found that prenatal stress affected the offspring's development in the cognitive, behaviour, and psychomotor domains. Human prenatal stress research is largely via prospective cohorts (O'Connor, Heron, Golding, Beveridge, & Glover, 2002) but many foundational studies retrospectively exploited populations who had been affected by natural or manmade disasters (Beydon & Saftlas, 2008). While lacking the stringent conditions of a lab design, prospective studies have the ability to recruit participants and manage data longitudinally, with prenatal stressors assessed by either by proxy (adverse life events, physical and mental health issues, etc.; Wisborg, Barklin, Hedegaard, & Henriksen, 2008; Seng, Sperlich, Low, Ronis, Muzik, & Liberzon, 2013) or by blood cortisol monitoring (Davis, Glynn, Waffarn, & Sandman, 2011). Retrospective studies have exploited previously collected maternal health data to compare against data collected from the offspring or collect recalled data from the participants for use in research with offspring.

Of contextual importance here are opportunistic studies following a population-level event. A ground-breaking work, the Dutch Hunger Winter project, is a generational study tracking the epigenetic health outcomes of participants *in utero* during the Nazi occupation-driven famine of 1944-45 and their descendants (Heijmans et al., 2008). A longitudinal study in a cohort of Finnish twins with prenatal exposure to the Chernobyl nuclear disaster found increased risk of depressive symptomology, Major Depressive Disorder, and ADHD at age 14 (Huizink, Dick, Sihvola, Pulkkinen, Rose, & Kaprio, 2007) and increased cortisol and testosterone levels in both genders at the same age (Huizink, Bartels, Rose, Pulkkinen, Eriksson, & Kaprio, 2008). Project Ice Storm has been following children with prenatal exposure to the Quebec ice storm (1998) that left several million Canadians without power for over a month. Participants were first assessed at 6 months (then on a 1-2 year schedule) showing the association of prenatal stress with

cognitive and developmental delay (Lapante et al., 2004; King & Lapante, 2005; Lapante, Brunet, Schmitz, Ciampi, & King, 2008), baseline cortisol elevation (Nguyen et al., 2018), externalising behaviour (Jones et al., 2019), obesity (Cao-Lei, Dancause, Elgbeili, Laplante, Szyf, & King, 2016), and other health outcomes. This study was unique in separating the mother's subjective experience of stress from objective stressors.

Many of the modifications discussed thus far have been type-dependent physiological adaptations to a specific expected environment that have functioned as deficits in non-severe environmental conditions. Animal models have shown very conclusive associations between prenatal stress and 'psychopathologies' (Beydoun & Saftlas, 2008) with human research also finding correlations, especially concerning HPA axis activation and its relationship with mental illness (Baumeister, Lightman, & Pariante, 2014; Kim, Bale, & Epperson, 2015). It has been proposed that prenatal stress constitutes an overall susceptibility rather than resulting in specific disorders (Huizink, Mulder, & Buitelaar, 2004) but it seems illogical that physiological changes would be type-dependent while psychological adaptations would simply be a 'catch-all' general risk. Lee and Goto (2013) argue that the deficits caused by prenatal stress can be considered adaptations to the stressful maternal environments. They highlight the issues of spatial learning/memory in the offspring of rats stressed by constant restraint, asserting that in an expected restraint environment, spatial learning/memory provides little benefit (as there is no escape from the stressor) but could be attuned to coping with restraint stress. In animal models showing sexual dimorphism, socially stressed guinea pigs bore female offspring who displayed more masculine traits and male offspring who displayed more docile, infantile traits (Kaiser, Kruijver, Straub, Sachser, & Swaab, 2003; Kaiser, Kruijver, Swaab, & Sachser, 2003). Kaiser and Sachser (2009) see this as an adaptation, with the dominant females more able to secure resources and the infantile males able to pass 'under the radar' of dominant males and survive to reproduce later, a theory with which Lee and Goto (2013) agree.

Social isolation/decreased social interaction during pregnancy would constitute a maternal stressor, with blood cortisol signalling this deficit environment to the foetus, triggering adaptations to the harsh environment. These modifications

would result in maladaptive behaviour in a normative setting but would mean the offspring would be more resilient to the effects of social isolation. Applying epigenetic principles to human psychopathology outcomes, Lee and Goto (2013) propose in their prenatal environmental adaptation hypothesis that prenatal stress in humans would produce type-dependant epigenetic adaptation in offspring which would contribute to psychopathology risk. Building on Kaiser and Sachser's (2009) work, they suggest that the epigenetic modifications occurring as a result of the prenatal environment (either normative or harsh), constitute type-dependent adaptations to the expected persisting environment which become maladaptive in other environments. The correlation between prenatal stress and increased risk for psychopathology should be considered evidence of a contribution to adverse mental health outcomes due to prenatal environmental adaptation (Lee & Goto, 2013).

1.5. Epigenetics and Psychopathology

Psychiatric disorders in the human population cannot be tied to a single causal factor and have persisted in the population for the length of recorded history despite being highly disadvantageous. It is well established that many of the 'major' psychopathologies carry moderate to high heritability (McGue, Iacono, & Krueger, 2006) with several 'candidate' genes implicated; *RBM12* and *COMT* in psychosis (Niarchou, Zammit, Escott-Price, Owen, & van den Bree, 2014; Steinberg et al., 2017), *COMT* in anxiety (Stein, Fallin, Schork, & Gelernter, 2005), and *5-HTT* in depression (Caspi et al., 2003). Polygenic risk, the interplay of several genes associated with psychopathology, can be used to predict disorder prevalence (International Schizophrenia Consortium, 2009; Dudbridge, 2013) as well. It must be noted that the genetic/polygenic effect is maintained after controlling for individual psychosocial covariates and systemic factors (Mullins et al., 2015; Duncan et al., 2019). It is already understood that epigenetic modifications can be passed down on either side of the genome and such effects can persist for several generations. The transgenerational transmission of trauma theory used in an epigenetic context, suggests that the trauma from one environment alters the genome of an individual who will then pass it on. This effect has been studied in Holocaust survivors and

their descendants (Yehuda & Bierer, 2007; Kellermann, 2013; Yehuda et al., 2014; Yehuda et al., 2016).

Epigenetic adaptations *in utero* to stressful/harsh prenatal environments may contribute to the variance in risk for psychopathology (Lee, Yamaguchi, & Goto, 2015). As such disorders would result in a reduced lifespan or decreased reproductive opportunities (Nanko & Moridaira, 1993; McGrath, Hearle, Jenner, Plant, Drummond, & Barkla, 1999; Cuijpers & Smit, 2002) in a prehistorical context, evolutionary theory dictates they should have been 'deselected' by natural/sexual selection long ago. Even in contemporary society, the traits and symptomology of mental illnesses carry stigma and disadvantage (Lee, Yamaguchi, & Goto, 2015). Adaptions to a severe environment would be out of place and maladaptive in a normative environment, registering as indicative of disorder. For example, a pregnant woman on the run from an abusive partner (stressor) births a child who shows hyperkinesis and hypervigilance in adolescence. Both are advantageous behaviours in an environment of evading a following danger but in a secure environment, they are maladaptive and symptomatic of ADD/ADHD or anxiety. This is why it is unwise to moralise 'adaptive' and 'maladaptive' in a human context, as even undesirable or distressing behaviour can be contextually adaptive. Paranoia is normally understood as a dimension of psychosis but paranoia while in prison is a matter of survival.

Considering psychiatric disorders solely in association with evolutionary theory instead of behavioural epigenetics can be problematic. Human society has existed for approximately 50,000 years (Klein, 1995), making it possible that environmental pressures have not been sufficient to force quicker adaptation or have not existed long enough to do so. Thus, working forward from a viewpoint of behavioural epigenetics, it is possible to examine the potential adaptive roots of psychopathology. Considering psychosis, it seems hard to imagine the symptomology as adaptive and yet, paranoia is a useful state in a threatening environment (as above; Raihani & Bell, 2019), delusional thought does not match reality but its processes show adaptive functioning (Mishara & Corlett, 2009), and audio/visual hallucinations can provide brain stimulation in abject isolation (Hoffman, 2007). Anxiety can be described as survival behaviour 'dialled up to 11',

particularly hypervigilance, excessive worry/fear, CNS arousal, and exaggerated startle response (Kunst & Winkel, 2013). Likewise, the social withdrawal of depression can be seen as protective measures during a time of vulnerability (Ike, de Boer, Buwalda, & Kas, 2020). In addition, variation in psychopathology presentation and expression, even intra-disorder, could be accounted for by variation in type and severity of prenatal stress (Lee & Goto, 2013).

The background literature has shown that i) prenatal stress can affect the foetal genome via epigenetic processes, ii) these adaptations can be type-dependent, iii) they are not solely physiological and psychological outcomes are possible, iv) behaviour resultant of these modifications constitute survival-driven adaptations which are maladaptive in a normative setting and, v) adaptations to specific environmental stressors could help explain some of the variance in the expression and presentation of specific psychopathologies. When applied to social environmental stressors, these findings suggest the presence of a 'social phenotype' created by prenatal stress. This project continued on from the prenatal maternal adaptation hypothesis (Lee & Goto, 2013; Lee, Yamaguchi, & Goto, 2015) and proposed that the stress of low prenatal maternal social contact/social isolation would trigger epigenetic mechanisms in the offspring to prime it for a severe, low social contact environment. As discussed above, Project Ice Storm took the innovative step of separating a mother's subject experience of stress with the objective occurrence of the stressor. Their findings indicate that in many circumstances, while subjective stress effects were more severe (Dancause, Laplante, Oremus, Fraser, Brunet, & King, 2011), the objective occurrence effects differed from an unaffected population (King & Laplante, 2005; Laplante, Brunet, Schmitz, Ciampi, & King, 2008). In considering the social environment, it was important to understand the nature of it as a potential stressor and if perception, reality, or both affected the epigenetic process.

1.6. Social Isolation as a Deficit Environment

In an evolutionary context, a harsh or deficit environment is not hard to define. Hard winters or summers producing extreme temperatures would make

prehistorical survival hard, worsened by the presence of predatory animals. Game animals moving on or a crop blight could mean starvation conditions while a drought could deplete the local groundwater. In these examples, the hostility of nature or the deficit of biological necessities is obvious, but these are not the only dangerous environments. Marcus Tullius Cicero is credited with the quote, "*Man is his own worst enemy*," (Cicero, 68-43BC/1806), which is true on both an individual and species level. A hostile environment can constitute a negative social environment and speaking socially, a deficit environment means isolation.

Abject isolation, being completely alone and without the presence of another human being, is easy to imagine. Social isolation, the experience of being alone while in the presence of others, is also familiar. Both situations can be equally terrifying and dangerous, depending on the context. Exile has been a popular punishment throughout history (Gorman, 1994; Finnane & McGuire, 2001) as the threat of facing the wilderness without the support or protection of others was, and remains, very serious. Likewise, deliberate social isolation (shunning), has also been used to reinforce social norms in many cultures and is still practiced today (Zippelius, 1986). However, it must be noted that often in contemporary society, an individual can find themselves in social isolation without it being deliberately practiced upon them. Moving to a new location without friends or family, being the sole elderly survivor of friends and family, or prioritising other endeavours over socialising; all can result in unintended social isolation. It is also possible for an individual to self-isolate for a variety of reasons, ranging from a preference for solitude, to the lasting effects of trauma, to suffering from mental or physical illness.

It might be argued that lack of food or water should not be considered alongside lack of social contact, but abject isolation is a deficit environment. The human body strives towards homeostasis and when it is lacking, it signals the individual to correct the imbalance. Hunger and thirst are indicators of insufficient food and water, with starvation and dehydration the result if those needs go unmet. It is interesting to note that in these extreme physical conditions, the body 'creates' its own food by digesting fat, muscles, connective tissue, and finally organs, and similarly 'creates' hydration by leeching it from any available tissue source, including the blood. These measures can prolong survival and increase survival

chances. When the brain is in deficit, it also signals in the hope of re-establishing homeostasis. Loneliness can be considered the equivalent of hunger or thirst, a sign that something is lacking (Cacioppo, Cacioppo, Capitanio, & Cole, 2015; Cacioppo, Cacioppo, Cole, Capitanio, Goossens, & Boomsma, 2015).

Mirroring the body, the brain in abject isolation also 'creates' its own stimuli. It is common for individuals in isolation to suffer audio and/or visual hallucinations (Ziskind, 1958; Zubek, Pushkar, Sansom, & Gowing, 1961; Kellerman, Rigler, & Siegel, 1977), an effect particularly noted in solitary confinement (Grassian, 1983; Haney, 2003). This relationship has led to new avenues of research concerning social isolation and adaptive psychopathology. The Social Deafferentation Hypothesis (Hoffman, 2007) proposes that sensory deprivation causes deafferentation (phantom limb pain, etc.) and that social isolation can cause similar deafferentation in the 'social brain', resulting in "*spurious social meaning in the form of complex, emotionally compelling hallucinations and delusions representing other persons or agents*." Social isolation and loneliness in a social deafferentation model has been implicated in increased hallucinations in both clinical and control populations (El Haj, Jardi, Larøi, & Antoine, 2016), formal thought disorder (De Sousa, Spray, Sellwood, & Bentall, 2015), anomalous bodily experiences in a schizophrenia (Michael & Park, 2016), and as a factor between trauma and psychopathology (Murphy, Shevlin, Adamson, & Houston, 2013; Shevlin, McElroy, & Murphy, 2014).

Even without the comparison to biological necessities, lack of socialisation and loneliness constitute a very real threat to the individual, as true now as it was in prehistory. Being lonely is associated with poor mental/physical health outcomes as well as increased all-cause mortality in older individuals (Luo, Hawkley, Waite, & Cacioppo, 2012). Holt-Lunstad, Smith, Baker, Harris, and Stephenson (2015) found on early mortality in a general population sample, including a statement much discussed in the media that loneliness is as detrimental to health as "*smoking 15 cigarettes a day*." It is also well demonstrated that social isolation and loneliness have adverse effects on an individual's mental health (Cacioppo & Patrick, 2008; Tew, Ramon, Slade, Bird, Melton, & Le Boutilier, 2012). Social contact has beneficial effects; the 'social environment' can mediate psychosis risk in

children/adolescents (Wicks, Hjern, Gunnell, Lewis, & Dalman, 2005; Singh, Winsper, Wolke, & Bryson, 2014), the distress of depression and anxiety (Zhou, Zhu, Zhang, & Cai, 2013; Roohafza et al., 2014), and increase psychological wellbeing (Hartup & Stevens, 1999; Deci, La Guardia, Moller, Scheiner, & Ryan, 2006).

The Dutch famine study has provided a wealth of information on the epigenetic impact of a severe deficit environment on offspring and their descendants. With food scarce and foetal nutrition lacking, children in the 1st trimester of development during the famine were born primed for a life on the edge of starvation but these adaptations were maladaptive in a normative environment (Schulz, 2010). The environmental mismatch of this population manifested as increased obesity risk (Phillips, Roseboom, Carroll, & de Rooij, 2012; Veenendaal et al., 2013), poor health outcomes in later life (Painter, Osmond, Gluckman, Hanson, Phillips, & Roseboom, 2008), and increased risk of coronary heart disease (Roseboom, 2000). Similarly, human beings literally need others to survive, as healthy brain development and maintaining mental/emotional homeostasis depend on socialisation and social contact (Blakemore & Choudhury, 2006; Johnson, Grossman, & Kadosh, 2009). Thus, an environment with little expectation of socialisation would constitute a considerable environmental stressor for a pregnant woman to navigate. Her own mental health and well-being would be at risk and the cortisol in her bloodstream, crossing the placental barrier to her foetus, would be enough to start the epigenetic process of preparing her offspring for survival in that harsh environment. Resilience to the psychological effects of this isolation would be beneficial to the child but only if the deficit environment persisted. If isolation ended as did the Dutch famine, leading to a child developing in a normative social environment, their ‘mismatch’ would manifest as distress and behaviour indicative of psychopathology, as type-dependent as the caloric-based health outcomes of the Dutch offspring.

Proposing this hypothesis in the abstract made for an interesting discussion but lacking evidence in the fossil record and the ability to (ethically) test it, such a theory was difficult to reliably evaluate. Sourcing data on prenatal maternal socialisation and offspring socialisation as the children developed was critical to accurately modelling these environments, as was having valid repeat measures for

offspring psychopathology. The Avon Longitudinal Study of Parents and Children (ALSPAC; 1991-present) had retrospective large population census type data which matched the needs of this project to follow a mother/child dyad from 8 weeks gestation through middle childhood. The decision was made to source this data in testing the thesis hypotheses and the ALSPAC methodology is explored in full in Chapter 2.

1.7. Thesis Overview

When considering evolutionary science, anything not supported by the fossil record or physical artefacts remain educated conjecture and as well-informed as that might be, there exists a substantial margin of error. This is as especially true for psychology, where no record of prehistoric thoughts, attitudes, or exact beliefs have survived. In testing the thesis hypotheses relating to evolutionary theory, it was crucial to use data that i) covered the entire time frame being examined (prenatal to middle childhood), ii) covered the constructs being tested (maternal and child socialisation, child psychopathology over time, and related psychosocial covariates), and iii) covered populations of sufficient size to yield valid analytical results even after 'longitudinal attrition'. While an experimental design would produce more valid results, both ethical considerations and time constraints meant that exploiting secondary longitudinal data, specifically collected by ALSPAC, was the best option to test these hypotheses.

This section will be an overview of the 5 empirical chapters detailing the aim of the chapter as it relates to establishing an analytical framework and the techniques used to fulfil that aim. Full methodologies feature in each corresponding chapter describing the data and analyses used during each step of the thesis process.

1.7.1. Chapter 3: Modelling the prenatal maternal social environment

To perform any testing involving the prenatal maternal social environment, it first needed to be statistically modelled and this model formed the foundation of the

analytical framework used to ultimately test the impact of this environment on child mental health outcomes. Self-completed maternal data describing the mother's social network and social support at 12 weeks gestation were sourced as the basis for this model. An exploratory factor analysis was run to determine the underlying dimensions of the prenatal maternal social environment. This technique was used rather than an exploratory structural equation model as the interest in this chapter was identifying the structure of the environment and not what predicted that structure as it was unrelated to the environment's effect on the child. The underlying dimensions of the prenatal maternal social environment could be conceptualised as the walls, floor, and ceiling of a room; it did not matter what influenced the colour of the walls, only what influenced how each member of the maternal cohort experienced that room. Having modelled this environment, it was then possible to use the dimensions to describe how the maternal cohort interacted with it.

1.7.2. Chapter 4: Specific profiles within the maternal population

Having created a factor model for the prenatal maternal social environment, the next phase of analysis focused on using those dimensions to define the maternal population's experience of that environment. Additional psychosocial covariate data were used to then explore what variables predicted specific experiences. A latent class analysis was conducted to identify discreet profiles (groups) within the maternal population with membership based on factor scores for the dimensions of the prenatal maternal social environment. This analysis resulted in a salient model describing different groups characterised by socialisation patterns. To explore the specifics of group membership, a bank of psychosocial covariates was used in a logistic regression. Extreme groups were examined against a baseline group to determine which covariates predicted class membership and to what extent. These profiles would be used as a proxy for the assumed 'social phenotype' resulting from differing socialisation in the prenatal maternal social environment, i.e. these profiles constituted the first determinant of environmental 'fit' required to test the environmental mismatch hypothesis.

1.7.3. Chapter 5: Modelling the childhood social environment

With a representation of the 'social phenotype' established, the next analytical phase focused on modelling the offspring social environment. As with the prenatal maternal social environment, the aim was to determine dimensional structure but unlike that analysis, this also sought to identify covariate indicators of the environment. Self-completed child data describing the child's social experiences and perceptions at age 9.5 years were sourced with a bank of both maternal and child psychosocial covariates, including the maternal socialisation profiles from Chapter 4. An exploratory structural equation model was tested to determine the factor structure of the child social environment (measurement component) and the relationship between that structure and the covariate indicators (structural component). This chapter established a cross-sectional model of the child social environment at age 9.5 years which could then be used to determine environmental fit between it and the prenatal maternal social environment.

1.7.4. Chapter 6: Modelling psychopathology across middle childhood

In order to determine the effect of the prenatal maternal social environment on offspring psychopathology, it was necessary to model that psychopathology and doing so longitudinally provided an opportunity to model change over time. The social environment was modelled as a 'snapshot' at age 9.5 years and so psychopathology was modelled as a trajectory between the ages of 7 and 11 years, with the social environmental measure falling at the mid-point of that span. Thus, it would be possible to determine child distress as a reaction to that environment. Parent-completed data on child behaviours were sourced at 3 time points; ages 7, 9, and 11 years and used in a 2-step analysis. A latent mixture model was tested against a null model to determine if there was change over time in the measure used. A latent growth mixture model was then tested to determine the number of trajectories in the population and their directionality. With psychopathology trajectories identified and child membership in these trajectories determined, the analytical framework had been completed in preparation for the final analysis to test the thesis hypotheses.

1.7.5. Chapter 7: Testing the impact of socialisation on psychopathology

The final step in this thesis was to test the impact of the prenatal maternal social environment on child mental health outcomes. As the crucial postnatal development period/early childhood is a time of heightened brain plasticity, a bank of maternal and child covariates known to contribute to psychopathology risk were included to control for their influence. A categorical variable was created describing environmental fit/mismatch with categories comprised of each possible combination of prenatal social environment and child social environment. A multinomial logistic regression was run, regressing the psychopathology trajectories onto the covariates to determine which, if any, were significant predictors. These significant covariates were included in a second multinomial logistic regression, regressing the psychopathology trajectories onto the environmental fit/mismatch categories and predictor covariates to determine the likelihood of trajectory based on prenatal maternal socialisation as modified by child socialisation. The results were then discussed in Chapter 7 (General Discussion).

1.8. Thesis Aims, Goals, and Justification

This thesis was both ambitious and fairly non-traditional, but it was built upon solid underlying theory, and used the methodologically reliable data of robust population cohorts in concert with powerful analytical techniques to test its hypotheses. The aim of this body of research was to unify elements of evolutionary, epigenetic, and personality theory with the biopsychosocial model of mental illness to challenge the conceptualisation of psychopathology risk. The goal of this project was to examine these disparate concepts by testing the impact of the prenatal maternal social environment on child mental health outcomes in a valid population. This was to be accomplished by creating an analytical framework with a replicable methodology so similar testing could be conducted in other population cohorts.

As was evident from Sections 3 and 4, epigenetics is a newer field with research implications that have inspired a boom in studies across multiple domains.

As behavioural genetics is an established field acknowledging the contribution of heritability to human behaviour, psychology, and psychopathology, behavioural epigenetics has become a natural extension of gene x environment research. Theories and hypotheses centring around potential psychological epigenetic effects, like the prenatal environmental adaptation hypothesis, are exciting in their implications. Thus, the primary justification of this thesis' existence was to contribute to this new field by testing the epigenetic impact of the prenatal maternal social environment on offspring child psychopathology in a novel way. Prospective behavioural epigenetic studies are a valuable scientific resource, but by their nature, take years or potentially decades to complete. A lesser justification for this work was to demonstrate that retrospective secondary data could also be used to validate behavioural epigenetic hypotheses, acting as theory support in the justification of 'real-time' longitudinal prospective studies.

While animal psychopathology model studies are economical and take less times to run, they can only go so far when discussing human psychology. Short gestational periods and the ability for multiple generations per study can yield quality biological/genetic results in small mammal prenatal stress studies but this type of research is not ethical to conduct on human participants. Opportunistic studies conducted during/after population stressor events have the benefit of longitudinal tracking of participants, but there is little value in waiting about for a population-level disaster to strike. There has been a call for the increased use of large population longitudinal studies to test epigenetic effects (Champagne & Mashoodh, 2009; Powledge, 2011; Notterman & Mitchell, 2015) and these studies should be exploited to the fullest extent. With the wealth of data available from ALSPAC, it was the perfect study to use in testing the hypotheses put forward here. In addition, the fact that its population is considered a representative sample of the greater UK population (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001), results here could be generalised past the study sample.

This thesis aimed to examine the potential epigenetic contribution of the prenatal maternal social environment to offspring psychopathology by i) modelling that environment, ii) defining discreet groups by their interaction with that environment, iii) modelling the offspring social environment, iv) examining

offspring psychopathology trajectories over time, and v) testing the impact of prenatal socialisation on offspring psychopathology as affected by child socialisation. This exploration was predicated on the hypothesis that if a physical harsh or deficit prenatal environment yields a foetal genome with epigenetic modifications designed to give the offspring the best chance of survival, the same would be true of a harsh or deficit social environment. It was predicted that offspring 'primed' for one type of social environment but who ended up in a differing type would experience distress, as manifested by psychopathology. Further, it was predicted that offspring who were born to a mother in prenatal social isolation would be more resilient to this environmental mismatch than the offspring of normative or highly prenatally socialised mothers. It was also hypothesised this effect would be present even after controlling for confounding factors during the postnatal period and would constitute a potential 'social phenotype'. Empirical testing of these hypotheses begins in Chapter 3, 'Modelling the Prenatal Maternal Social Environment'.

1.9. Introduction References

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Chapter 2

ALSPAC in theory and in practice

2.1. Introduction

Retrospective secondary data from the Avon Longitudinal Study of Parents and Children (ALSPAC; 1991-current) comprised the whole of this project. What follows is an overview of ALSPAC purpose, aims, and methodology to give a broad understanding of its generational undertaking. The value of such studies cannot be overstated, and it was the sheer wealth of data and strength of design that made ALSPAC particularly appropriate for use in the design of this thesis. This section outlines the major methodologies of the study while specific methodologies including scales and sub-section design are described in their relevant empirical chapter. This information was sourced from published guides on the maternal and child cohorts (Fraser et al., 2013 and Boyd et al., 2012, respectively), the study methodologies compiled by members of the ALSPAC project (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001; Golding & the ALSPAC Study Team, 2004), and project updates (Boyd et al., 2019).

2.2. Aims

ALSPAC was conceived as a long-term, multi-generational study to investigate interactions between the individual genome and the environment, specifically concerning health outcomes (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001). ALSPAC was also designed as a cohort of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC), itself a multinational large-population census-style longitudinal study examining development and health outcomes (Boyd et al., 2012). ALSPAC goals included detailing mechanisms that underlie these environmental interactions, potentially leading to a greater understanding of health and behaviour throughout the lifespan (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001; Golding & the ALSPAC Study Team, 2004). Currently, the study has begun collecting data on the 3rd generation of participants (University of Bristol, 2020a) and to date, over 2,000 studies have been published using ALSPAC data in a variety of fields and disciplines (University of Bristol, 2020b). ALSPAC receives the bulk of its funding from the University of Bristol, the UK Medical Research Council (MRC), and the Wellcome Trust with

additional funding provided by various smaller funders (University of Bristol, 2020c).

2.3. Overall Design

The main design of ALSPAC was an in-depth examination of the major and minor factors that influenced life outcomes and the mechanisms driving these processes. This was a very thorough project which has made the attempt to catalogue every variable of potential significance, even if that significance was not immediately apparent. Figure 1 (Golding & the ALSPAC Study Team, 2004) illustrates the 'road map' of ALSPAC study aims. Environmental influences on development occupied 8 major domains: psychosocial conditions and parenting, diet and lifestyle, environmental pollutants, housing, health behaviour, medical and dental care, day care, and schooling. It was generally accepted that these domains produced environmental interactions, not only with each other but also the individual genome (Golding & the ALSPAC Study Team, 2004), that in turn influenced specific outcomes ranging from physical health, to mental health and wellbeing, to overarching sociological issues. These relationships were described as 'influences' and 'contributory factors' in all literature, including those written for the general public. While it is an unwritten rule in the social sciences to avoid direct causal attributions, it was important to keep in mind public interest concerning this research and the ability of the public (and media) to misinterpret research results.

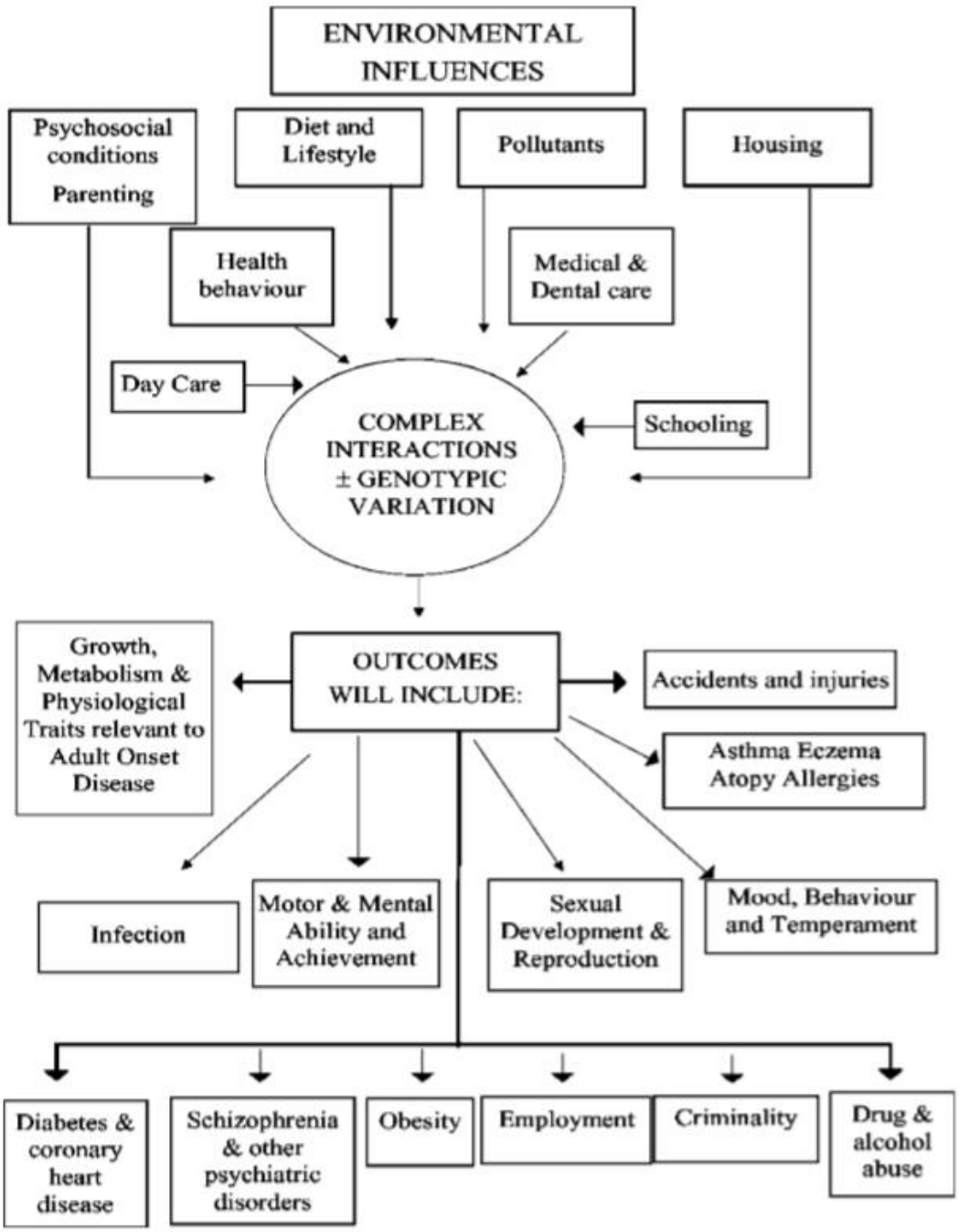

Figure 2.1. ALSPAC study aims (Golding & the ALSPAC Study Team, 2004)

2.4. Sample

2.4.1 Study area

The ALSPAC study area was defined as a portion of Avon County bordering on the Severn estuary, roughly 120 miles west of London and including the city of Bristol and excluding Bath. This area comprised 3 health administration districts within the South West Regional Health Authority (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001; Golding & the ALSPAC Study Team, 2004; Boyd et al., 2012). In 1991, this area contained a population of approximately 1 million (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001) and was chosen after analysis of the longitudinal Children and Health Education Study (CHES; Bakker et al., 2015) showed this population to be not atypical from the rest of the country in a multitude of factors including heterogeneity in socioeconomic backgrounds, housing, and a featured both urban and rural communities (Golding & the ALSPAC Study Team, 2004). It was further considered that the ALSPAC study area population could be considered a representative sample of the United Kingdom (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001; Boyd et al., 2012), allowing results from the data to be generalised to the population as a whole.

2.4.2. Eligibility, recruitment, enrolment, and attrition

Any pregnant woman within the study area with an expected delivery date between 1st April 1991 and 31st December 1992 was considered eligible for participation, with recruitment beginning in September 1990. This is considered the ‘first wave’ of the overall ALSPAC study, named ‘Children of the 90s’ and designated with a logo featuring a hot air balloon. Some aspects of recruitment eligibility were described retrospectively as developing technology made such designations possible (see Boyd et al., 2012).

Recruitment efforts followed consultations with local medical professionals and were widespread, following many different avenues of outreach to encourage

enrolment. These efforts included: press coverage (radio and television) on both a local and national scale, professional cooperation by midwifes and hospitals, ALSPAC staff approached eligible women at routine medical appointments and after delivery, and posters placed in any place a newly pregnant mother might frequent (see Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001). Most outreach methods provided an informational card for the mother to fill out with her name, DOB, address, date of last menstruation, and expected due date, and return by post. On receipt on this card, the ALSPAC office sent out an informational packet explaining the scope and aims of the study, the types of information that would be gathered (along with ethics considerations and data privacy), that the participant would be free to leave the study at any time, and that she would be considered enrolled unless she made contact to opt out.

The first wave of recruitment was not the only intake of participants (Figure 3). A second effort was made to identify eligible pregnancies from 1991-1992 where no recruitment engagement occurred or was incomplete, coinciding with the age 7 follow-up data collection (focus@7), and invite these women and children to participate. A third recruitment outreach program sought to contact more potentially eligible families that might have been missed or failed to follow-up with enrolment in the initial wave. Exceptions here were any women who opted out of the study and requested not to be contacted further. It must be noted that for participants who joined in the second and third phase, prenatal, infancy, and childhood data was not collected (Boyd et al., 2012).

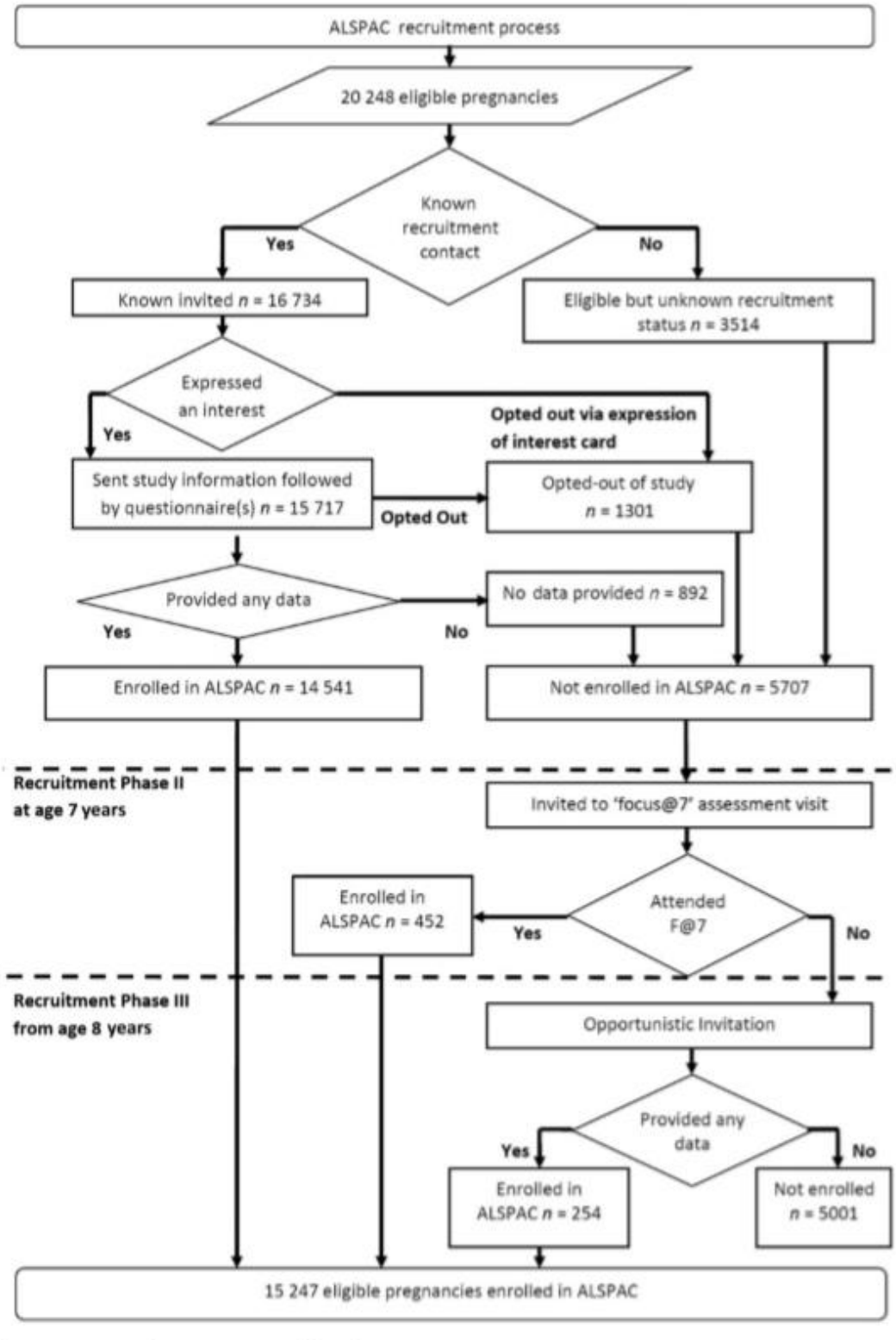

Figure 2.2. ALSPAC recruitment workflow (Boyd et al., 2012)

Attrition is an issue in any study with more than 1 timepoint interaction and it was expected due to the generational longitudinal nature of ALSPAC. The highest

rates of absolute attrition occurred during study child infancy and the transition to adulthood though partial attrition has been noted with active participants missing some repeated measures (Boyd et al., 2012). Some incomplete information has been addressed via follow-up with inactive members over age 18 and pursuing health record linkage directly from the NHS for unreachable inactive participants (Boyd et al., 2012; 2019). The total absolute attrition from birth to 18+ for this cohort was 2,018 untraceable and 782 withdrawn (Boyd et al., 2012).

2.4.3. Mortality

ALSPAC accepted notification of miscarriage, stillbirth, or later death of the infant/child from the mother (or family member), nurse/midwife/professional from the gynaecological ward, independent midwife/carer, or local pathologist. ALSPAC policy in such events was to send condolences to the mother from the study and invite her to provide a bit more information, if willing. If so, follow-up questionnaires were dependant on the age of the deceased. An environmental survey was sent 3 weeks after foetal death with a follow-up at 8 weeks on the mother's feelings around the event and support she received. A version of this second questionnaire was sent 8 weeks following stillbirth or infant death. In the event of later death, follow-up questionnaires were more in-depth concerning the time preceding the death as well as the emotional and support follow-up (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001). As of 2012, morbidity in the 1st generation child cohort was 100 (N=53 (4 weeks to ≤2), N=24 (>2 to <7), N=10 (<7 to >7), N=5 (>7 to <13), N=3 (≥13 to ≤16), N=5 (>16 to ≤18)), with N=614 miscarriages or stillbirths (Boyd et al., 2012).

Maternal deaths have been recorded via direct contact with ALSPAC but were also noted via health record links to the NHS Central Register, which provided date of death and cause, in addition to cancer and emigration data (Fraser et al., 2013).

2.4.4. General cohort demographics

Mean age for the maternal population was 27.77 years (SD=4.91 years) with a range of 15-45. Most respondents had an established history in the Avon catchment area; 53.4% had lived in/near Avon all their lives, 16.9% over 10 years, 11.2% between 5 and 9 years, 13.6% between 1 and 4 years, and 5% for under a year (Herrick, Golding, and the ALSPAC Study Team, 2008). The population was further described as 79.1% homeowners, 79.4% married, and 97.8% were white/Caucasian (Fraser et al., 2013). Analytic sample sizes by chapter are shown in Figure 2.3.

In describing the child cohort population at birth, 49.69% were female, 96.09% were white, and 6.22% came from a low-income household (Boyd et al., 2012). Analytic sample sizes by chapter are shown in Figure 2.3.

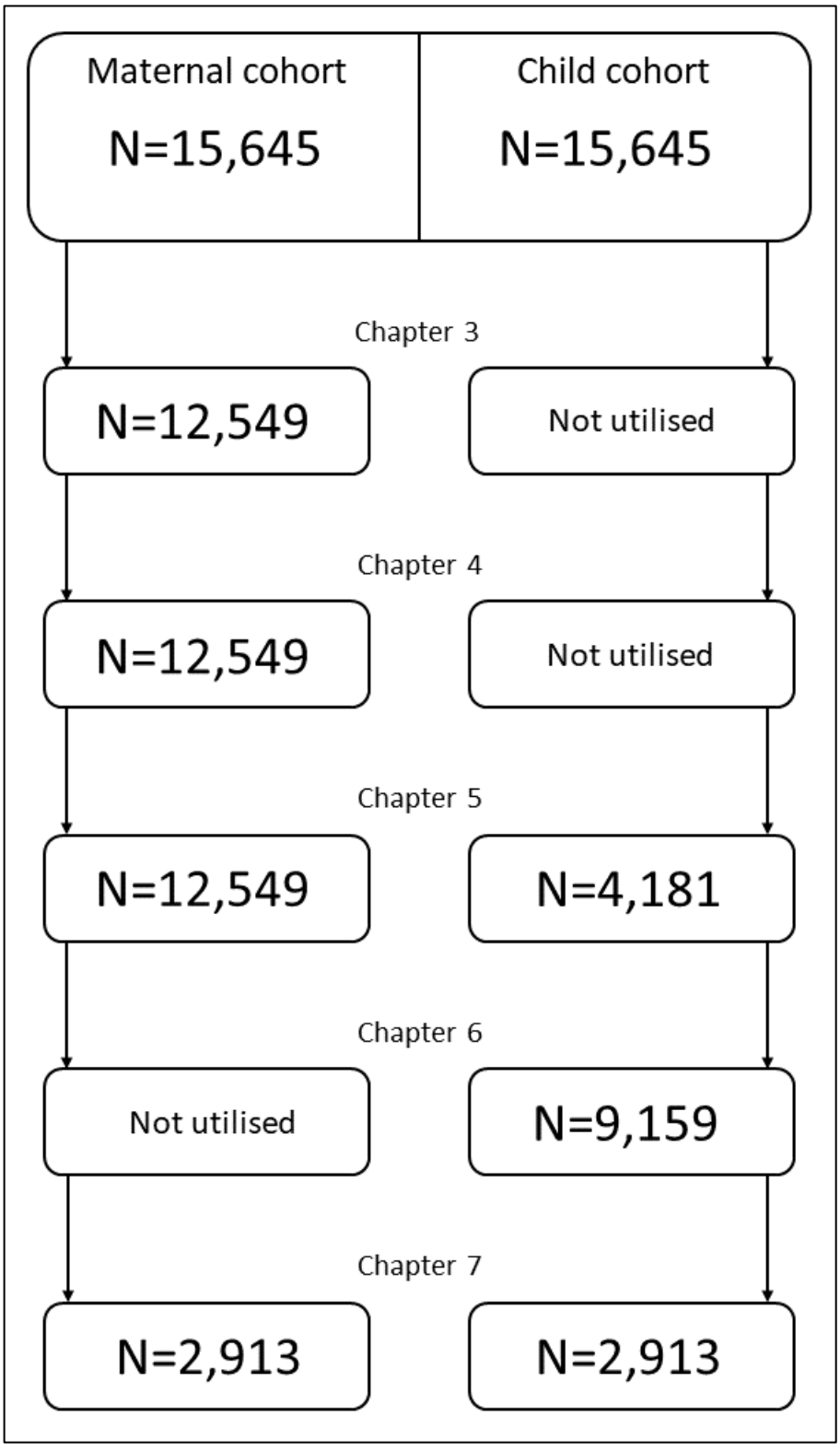

Figure 2.3. Analytical sample sizes of ALSPAC cohorts by chapter

2.5. Measures

Data collection for the first wave consisted of 80,977 separate variables (University of Bristol, 2020d) which are available for research use. These measures include but are not limited to demographic, environmental, genetic/epigenetic, biometric/physical, psychological, educational, and socioeconomic factors. Many variables are repeat measures on fixed schedules due to ALSPAC's longitudinal design. Measures used in this thesis are covered below in their sequential order of use in each empirical chapter, with socio-demographic variables described in Table 2.1.

Table 2.1. Descriptive statistics for main maternal socio-demographic variables

	N	Range	Mean	Standard Deviation
Maternal age (at delivery)	13,512	15-45	27.77	4.91
Socioeconomic status	11,121	1-7	3.87	1.97
Neighbourhood quality	13,041	0-12	8.08	2.27

2.5.1 Chapter 3 measures and variables

Chapter 3 featured a factor model based on items taken from a larger, 20-item scale originally designed for use by ELSPAC (Prokhorskas, Ignatyeva, Dragonas, & Golding, 1989) and influenced by qualitative research undertaken by Thalia Dragonas in a cohort of Greek mothers (Dragonas, 1987; Thorpe, Dragonas, & Golding, 1992). This scale appeared in the 'About Yourself' self-completion questionnaire given to the mothers at 12 weeks gestation. As used by ALSPAC, this scale consisted of 10 items concerning social networking (α=0.728) and 10 items concerning social support (α=0.575), with each section summarised by an aggregate sub-score by item value sum after several items were recoded (Herrick, Golding, & the ALSPAC Study Team, 2008). The sub-scores were not used in this model as itemisation provided a more nuanced picture of the maternal prenatal social environment. The overall reliability for the combined scale was α=0.314 and α=0.642 for the combined sub-scores.

To better summarise the data, 3 items were dropped from the social network sub-scale (‘number of relatives seen at least twice in the past year’, ‘member of a close circle of friends’, and ‘number of people to borrow £100 from’). The item concerning relatives was dropped as being too close to another item (‘meetings with relatives in the past month’) as that item better captured relative social exposure during gestation, rather than before it. An item regarding a close circle of friends was the sole binary variable and was dropped to preserve scale parsimony. Finally, it was felt that the social support sub-scale’s monetary items better convey the expectation of support over the above item; an individual may have several friends/family who would be willing to help with money but their socio-economic status might preclude lending £100 (£210.90 in 2018, adjusted for inflation; Bank of England, 2019).

In addition, 4 items were dropped from the social support sub-scale (‘partner provides emotional support needed’, ‘worried that partner might leave’, ‘when tired can rely on partner’, and ‘state would help with money’). The ‘partner’ items were dropped from this phase of analysis for several reasons; data inconsistency as some respondents stated they had no partner but answered the ‘partner’ items anyway, the role of the partner is not integral to either the contributing theories nor the model, and other items in the scale feature ‘someone’ who could be a partner, but also a friend or relative (example: ‘no one to share feelings with’ and ‘someone to share the excitement of pregnancy’). The item on expectation of state support was dropped as irrelevant to the mother’s social environment. Reliability for the truncated scale was α=0.195.

Items were presented in Likert type format. For the 7 continuous variable items (‘number of friends’, ‘number of people to confide in’, ‘number of people who confide’, ‘meetings with friends in the last month’, ‘meetings with relatives in the last month’, ‘number of people to discuss decisions with’, and ‘number of helpers if in trouble’), response options were categorical and scored 1-4 (‘none’, ‘1’, ‘2-4’, and ‘>4’). The remaining items (‘no one to share feelings with’, ‘other pregnant women to share experiences’, ‘someone to share excitement of pregnancy’, ‘neighbours would help if in difficulties’, ‘family would help with money’, and ‘friends would help with money’) used attitudinal response options scored 1-4 (‘this is exactly how I feel’, ‘this is often how I feel’, ‘this is sometimes how I feel’, and ‘I never feel this

way'). Any responses outside the Likert scale were noted during ALSPAC data coding and were set to 'missing' (Herrick, Golding, & the ALSPAC Study Team, 2008). The exact wording of these items is quoted in Table 3.1.

2.5.2. Chapter 4 measures and variables

Chapter 4 featured a latent profile analysis of the maternal cohort based on the socialisation factors derived in Chapter 3, which were then regressed onto a bank of predictor covariates (socioeconomic status, neighbourhood quality, interpersonal sensitivity, adverse life events, discrimination, depression, home stability, abuse, presence of a partner, and age) in a multinomial logistic regression. Covariate data was sourced from the mother-based self-complete prenatal questionnaires 'Your Environment' (8 weeks gestation), 'About Yourself' (12 weeks gestation), 'Having A Baby' (18 weeks gestation), and 'Your Pregnancy' (32 weeks gestation).

The mother's socioeconomic status (SES) data was collected by occupation proxy questions over 7 surveys (12-, 18-, and 32-weeks' gestation, 8, 21, 33, and 47 months). During ALSPAC coding, these data were then cleaned, validated, and processed using the CASCOT (Computer Assisted Structured COding Tool; Jones & Elias, 2004) software for semi-automatic analysis and classification, with a 10% human audit confirming a low error rate (<5%). Results were standardised into multiple economic classification schema, including the National Statistics Socio Economic Classification (NS-SEC), and checked against data from the Institute for Social and Economic Research (ISER). The simplified NS-SEC was used in this analysis and consisted of 1-7 classifications, coded for use as 1='higher managerial, administrative, and professional occupations', 2='lower managerial, administrative, and professional occupations', 3='intermediate occupations', 4='small employers and own account workers', 5='lower supervisory and technical occupations', 6='semi-routine occupations', and 7='routine occupations'). It is important to note that SES/social class schemas are approximations of an individual's status based on proxy variables. (The ALSPAC Study Team, 2015)

Neighbourhood quality was a derived score based on a scale measuring the respondent's perceptions and attitudes surrounding relationships with neighbours, neighbourhood crime, and overall safety. Neighbourhood quality was assessed at 8 weeks gestation with a 19-item scale designed by the Home Office for use in the CHES survey (Bakker et al., 2015). Overall opinion of the neighbourhood was assessed and scored in Likert type format ranging from 1-4 ('very good area', 'fairly good area', 'not very good area', and 'bad area'), followed by 8 items detailing the mother's positive and negative situational interactions with neighbours, ranging from 1-5 ('never', 'rarely, 'sometimes', 'often', and 'always'). An additional 4 items addressed the mother's worries concerning possible burglary, mugging & robbery, sexual assault/pestering, and vandalism, ranging from 1-4 ('very worried', 'fairly worried', 'not very worried', and 'not worried'). The last 6 items below concerned neighbourhood attributes, ranging from 1-3 ('usually', 'sometimes', and 'never'). During ALSPAC coding (Herrick, Golding, & the ALSPAC Study Team, 2008), items 1-4 were recoded as (1=2, 2=1, 3=0) and items 5 and 6 were recoded as (1=0, 2=1, 3=2). All items were summed to produce a neighbourhood quality score with a higher score indicating a better neighbourhood. Neighbourhood quality was coded and used as a continuous variable.

1. Is your neighbourhood lively?
2. …friendly?
3. …noisy?
4. …clean?
5. …attractive?
6. …polluted/dirty?

Interpersonal sensitivity was also a derived score from Boyce and Parker's 36-item Interpersonal Sensitivity Measure (IPSM, Boyce & Parker, 1989), consisting of 5 dimensions of this construct: interpersonal awareness, need for approval, separation anxiety, timidity, and fragile inner-self. While all 5 sub-scores describe issues in relating to others, the overall score describes the whole of the construct. The IPSM was given at 12 weeks gestation. Items in this measure are scored from 1-4 ('very like me', 'quite like me', 'quite unlike me', and 'very unlike me'), and recoded (1=4, 2=3, 3=2, 4=1) to be summed to yield a sub-scale score. The

inventory total score is a sum of all sub-scale scores and a higher score indicates a lower measure of interpersonal sensitivity. Interpersonal sensitivity was coded as a continuous variable. This inventory was used by ALSPAC due to its validity as a correlate for neuroticism and predictor for post-partum depression (Bishop, Herrick, Stowe, Golding, & the ALSPAC Study Team, 2008).

Adverse life events since conception were measured twice, at 12 and 32 weeks gestation, and consisted of a list of 41 events and a text entry for any other event that affected the respondent but was not listed (see Appendix D). Events were scored by descending effect on the respondent from 1 (‘yes & affected me a lot’) to 4 (‘yes, but did not affect me at all’), with the option to select 5 (‘no, did not happen’). Scores were recoded as (1,2,3,4=1) and (5=0) for a total life events score and recoded (1,2,3,4=4,3,2,1) and (5=0) for a weighted total life events score (Bishop, Herrick, Stowe, Golding, & the ALSPAC Study Team, 2008). This analysis used the weighted total life events score, which was scored as a continuous variable.

Information on discrimination was taken at 18 weeks gestation. Discrimination represented any instance of perceived discrimination in the past year on the basis of sex, skin colour/ethnicity, clothing, family background, speech/accent, religion, or any other reason not mentioned. These questions were based on a sub-survey designed by the Home Office for the CHES study (Bakker et al., 2015). Discrimination was scored as a binary variable with 1=yes, 0=no. Depression was measured at 32 weeks gestation in the form of a general medical and mental health survey in which mothers were asked if they had ever suffered ‘severe depression’. This was scored as a binary variable with 1=yes, 0=no.

An additional covariate, Home Stability, described respondents’ childhood situation. A series of 4 items was asked at 32 weeks gestation covering the ‘reliability & stability’ of the respondent’s mother, father, mother figure, and father figure in a scale of 1-4 (‘very stable’, ‘fairly stable’, ‘unstable’, and ‘very unstable’). Home stability was a derived variable from these 4 items. Stability was set at 1 (‘very stable’) and reset to match the highest response from the preceding items, coded as 1=’very stable’, 2=’fairly stable’, 3=’unstable’, 4=’very unstable’. During

ALSPAC coding (The ALSPAC Study Team, 2009b), home stability was coded and used as a categorical variable.

1. Was your mother's behaviour stable and predictable to you as a child?
2. …your father's behaviour?
3. …your mother figure's behaviour?
4. …your father figure's behaviour?

Questions concerning abuse were asked at 18 weeks gestation and involved a section of 7 items designed for ALSPAC by the study team and Dr. Jean Price (Bickerstaffe et al., 2008). This variable was recorded as any instance of sexual abuse and coded as abuse from a stranger, a non-stranger, or did not occur. For use in this analysis, abuse (stranger) and abuse (non-stranger) were considered separate binary variables and coded as 1=yes, 0=no.

The presence of a partner was taken from the Social Network and Support scale asked at 32 weeks gestation (Prokhorskas, Ignatyeva, Dragonas, & Golding, 1989) and was coded and used as a binary variable (1=yes, 0=no). Age was recorded at 8 weeks gestation and coded as a continuous variable with the outliers ≤15(n=17) and ≥45(n=3).

2.5.3. Chapter 5 measures and variables

Chapter 5 involved an exploratory structural equation model (ESEM) to determine the factor structure of the social environment for the child cohort. This model was based on a self-complete measure given to the cohort, which was then regressed onto a bank of indicator covariates. These covariates were taken from maternal self-complete surveys and child-based surveys completed by the mother.

2.5.3.1. Child measures and variables

Child-completed surveys were written with a child's comprehension in mind and feature non-clinical, age-appropriate language. 'My Hands, My Feet, and Me' (9.5 years), was comprised of a series of 76 questions in 2 sections, covering self-image/relationship with parents/school performance and hand/foot/eye preferences.

The analysis in Chapter 5 used 8 items from the first section of this survey. These items covered friends/friendship and were taken here to form a scale describing socialisation. Reliability (α=0.691) was on the threshold of acceptable, which may have been due to the limited number of items in the scale (Tavakol & Dennick, 2011). Items were scored in Likert format from 1-5 ('not true', 'mostly untrue', 'partly true', 'mostly true', and 'true'). During ALSPAC initial coding, these items were coded and used as categorical variables.

1. I have lots of friends.
2. I make friends easily.
3. Most kids have more friends than I do.
4. I get along with kids easily.
5. Other kids want me to be their friend.
6. I have more friends than most other kids.
7. I am popular with kids of my own age.
8. Most other kids like me.

Child covariates were taken from child-based surveys. The child's gender was taken directly from the core sample data and this information was taken from birth records and notifications (Boyd et al., 2012). Gender was coded as a binary variable with 1=male, 2=female.

This analysis utilised adverse life events data over several points from ages 18 months through 8.5 years. Repeat variables were taken from the mother-completed child-based surveys 'Boy/Girl Toddler' (18 months) 'My Study Son/Daughter' (2.5 years), 'My Son/Daughter's Health and Behaviour' (3.5 years), 'Development and Health of My Son/Daughter' (5 years), 'My School Boy/Girl' (6

years), ‘My Son/Daughter at School’ (7 years), and ‘My Son/Daughter at Home and at School’ (8.5 years). This scale was presented as ‘upsetting events’ and consisted of a 15-item inventory of adverse life events. These were scored in Likert type format concerning event occurrence, ranging from 1-5 (‘yes and child very upset’, ‘yes and child quite upset’, ‘yes and child a bit upset’, ‘yes but child wasn’t upset’, and ‘no, it did not happen’). This analysis utilised 3 items from this scale at the above time-points:

1. Child was taken into care.
2. Child was physically hurt by someone.
3. Child was sexually abused.

During ALSPAC coding (Dewey, Stowe, & Golding, 1996; Golding, Cripps, Stowe, & Bishop, 1997; Golding, Bickerstaffe, Heron, Stowe, & Bishop, 2003; The ALSPAC Study Team, 2006; The ALSPAC Study Team, 2007a; Northstone, Herrick, Wilson, Golding, & the ALSPAC Study Team, 2004; The ALSPAC Study Team, 2007b), these items were re-coded as (1=1, 2=1, 3=1, 4=1, 5=0) with 1=yes, 0=no and combined into a single binary variable for each time point with 1=yes, 0=no. With this use, 1 indicated the occurrence of any of the 3 events at that time point and 0 indicated that none of them had occurred. This variable was coded and used as a binary variable.

2.5.3.2. Maternal measures and variables

Several maternal covariates were incorporated into this analysis, sourced from the mother-based self-complete prenatal questionnaires ‘About Yourself’ (12 weeks gestation), ‘Having A Baby’ (18 weeks gestation), and ‘Your Pregnancy’ (32 weeks gestation). These included the presence of a partner, SES, neighbourhood quality, and home stability, which are described in Section 2.5.2 above. Two covariates were derived variables from Chapter 3: membership in the High Socialisation profile and membership in the Low Socialisation profile.

The final 2 maternal covariates were membership in the High Socialisation profile and the Low Socialisation profile defined in Chapter 3. These were both binary variables scored as 1=yes, 0=no.

2.5.4. Chapter 6 measures and variables

Chapter 6 featured a latent mixture model and latent mixture growth model based on the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) which was given to the maternal cohort at study child ages 7, 9, and 11 years as part of child-based surveys. 'My Son/Daughter at School' (7 years) covered general health, life events, physical/cognitive abilities, family dynamics, and food/drink (Northstone, Herrick, Wilson, Golding, & the ALSPAC Study Team, 2004). 'My Son/Daughter at 9' (9 years) covered school/education, discipline and lifestyle, communication, family interactions, moods/feelings, sleep, physical measures, toilet use, and food/drink (The ALSPAC Study Team, 2007). 'Being a Boy/Girl' (11 years) covered general health, developmental issues, accidents/injuries, discipline/lifestyle, medications, moods/feelings, school, child's listening abilities, activities, and cultural influences (The ALSPAC Study Team, 2007).

Goodman (1997) based the SDQ in part on the Rutter child behaviour questionnaire (Rutter, 1967), outlining 5 main domains identified via factor analysis; prosocial behaviour, hyperactivity, emotional symptoms, conduct problems, and peer problems. While well-used and validated, the Rutter questionnaire only measured difficulties, not strengths, and used a threshold of 'cases' verses 'non-cases' in potential diagnosis (Goodman, 2001). The goal of the SDQ was to be a comprehensive inventory for children ages 4-16 which captured both strengths and difficulties across 5 dimensions (Goodman, 1997). This tool could be given to parents and teachers but also to children, and a version was developed for use with adolescents 11-16 (Goodman & Scott, 1999). Repeated analysis in multiple populations have found the SDQ to possess high internal reliability, parent-child agreement, statistical validity, and that it is a reliable predictor of child psychopathology (Goodman, 2001; Muris, Meesters, & van den Berg, 2003). If only one source is available for use with the SDQ, the parents are the most reliable

choice, as parental ratings are more predictive of emotional disorders than teacher or over-11 child self-report data (Goodman, Ford, Simmons, Gatward, & Meltzer, 2000). Reliability for the sub-scores and total score in this sample fell into the acceptable range (Tavakol & Dennick, 2011): Prosocial (α=0.858), Hyperactivity (α=0.862), Emotional Symptoms (α=0.863), Conduct Problems (α=0.863), Peer Problems (α=0.867), and Total Difficulties (α=0.883).

SDQ items and ALSPAC recoding information are shown in Table 2.2. Each item asked the parent to consider and answer as was appropriate to the child's behaviour within the past 6 months. This analysis utilised 4 of the domain sub-scores and the Total Difficulties score. Each sub-score was derived from 5 items scored in Likert format from 1-3 ('not true', 'somewhat true', and 'certainly true') and recoded during ALSPAC data recording. These items were then summed to produce each sub-score which ranged from 1-10 and was coded and used as a continuous variable. The Prosocial score was not utilised in the final model as socialisation was previously modelled using a scale which more accurately represented this construct. The 4 difficulty sub-scores were summed to produce the Total Difficulties score, with higher scores indicating greater difficulties experienced by the child. This variable ranged from 0-40 and was coded and used as a continuous variable.

Table 2.2. Strengths and difficulties questionnaire items and ALSPAC recoding information

Item	Recoding
Prosocial	
Child has been considerate of other people's feelings.	1=0, 2=1, 3=2
Child has shared readily with other children.	1=0, 2=1, 3=2
Child is generally obedient and usually does what adults request.	1=0, 2=1, 3=2
Child is helpful if someone is hurt, upset, or feeling ill.	1=0, 2=1, 3=2
Child often volunteers to help others (parents, teachers, other children).	1=0, 2=1, 3=2
Hyperactivity	
Child has been restless/overactive/cannot sit still for long.	1=0, 2=1, 3=2
Child has been constantly fidgeting or squirming.	1=0, 2=1, 3=2
Child has been easily distracted, concentration wandering.	1=0, 2=1, 3=2
Child has thought things out before acting.	3=0, 2=1, 1=2
Child has seen tasks through to the end, had good attention span.	3=0, 2=1, 1=2
Emotional symptoms	
Child has often complained of headaches/stomach aches/sickness.	1=0, 2=1, 3=2
Child has many worries, often seems worried.	1=0, 2=1, 3=2
Child has often been unhappy/down-hearted/tearful.	1=0, 2=1, 3=2
Child has been nervous or clingy in new situations, easily lost confidence.	1=0, 2=1, 3=2
Child has had many fears, easily scared.	1=0, 2=1, 3=2
Conduct problems	
Child has often had temper tantrums or hot tempers.	1=0, 2=1, 3=2
Child has often fought with other children or bullied them.	1=0, 2=1, 3=2
Child has often lied or cheated.	1=0, 2=1, 3=2
Child has stolen from home/school/elsewhere.	1=0, 2=1, 3=2
Child has been generally obedient, usually does what adults request.	3=0, 2=1, 1=2
Peer problems	
Child is rather solitary, tends to play alone.	1=0, 2=1, 3=2
Child has been picked on or bullied by other children.	1=0, 2=1, 3=2
Child has gets on better with adults than other children.	1=0, 2=1, 3=2
Child has had at least one good friend.	3=0, 2=1, 1=2
Child has been generally liked by other children.	3=0, 2=1, 1=2

2.5.5. Chapter 7 measures and variables

Chapter 7 featured a regression analysis including several thesis-derived variables, child covariates, and maternal covariates.

2.5.5.1. Thesis-derived variables

For the analysis in Chapter 7, 3 of the measures used were derived variables from previous phases of the project, socialisation profile membership for the maternal cohort, rate of socialisation in the child cohort, and trajectory of psychopathology over middle childhood.

The underlying structure of the prenatal maternal social environment was determined in Chapter 2 by using a 13-item scale given at 12 weeks gestation which described social interactions and expectations in the maternal cohort. The resultant 5-factor model was composed of the dimensions *Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support*. Factor scores along these dimensions determined each individual's membership in 3 latent profiles derived in Chapter 3: Baseline Socialisation, High Socialisation, and Low Socialisation profiles. With the Baseline Socialisation profile as a reference, membership in the High Socialisation profile was predicted by higher SES and neighbourhood quality, lower interpersonal sensitivity and adverse life events, and the presence of a partner. Membership in the Low Socialisation profile was predicted by lower SES and neighbourhood quality, a higher number of adverse life events, and the experiences of discrimination and severe depression.

The underlying structure of the child social environment was identified in Chapter 4 by using an 8-item scale given to the child cohort at age 9.5 years which described social interactions and perceptions of socialisation. It was determined that the underlying structure of the child social environment was a unidimensional construct of Socialisation. Higher rates of Socialisation were predicted by maternal childhood home stability and the mother's membership in the High Socialisation profile. For use in this analysis, the child cohort was divided into tertiles based on rates of socialisation, yielding a 1st, 2nd, and 3rd tertile group labelled as Low, Medium, and High socialisation.

A variable was created to define the combination of prenatal maternal social environment and child social environment by removing the probabilistic aspects of group membership and 'snapping' members into definite profiles, partnered with the

child's socialisation tertile. The resultant variable described both the maternal and child socialisation as membership in a specific category:

1. maternal low/child low (MLCL)
2. maternal medium/child low (MMCL)
3. maternal high/child low (MHCL)
4. maternal low/child medium (MLCM)
5. maternal medium/child medium (MMCM)
6. maternal high/child medium (MHCM)
7. maternal low/child high (MLCH)
8. maternal medium/child high (MMCH)
9. maternal high/child high (MHCH)

Change in psychopathology over time was determined in Chapter 5 by using the problem sub-scores and Total Difficulty score from the Strengths and Difficulties Questionnaire (SDQ, Goodman, 1997), given to the maternal cohort at child ages 7, 9, and 11 years. In a linear growth mixture model, 4 latent classes with unique trajectories of psychopathology were identified: Stable Low, Stable High, Increasing, and Decreasing difficulty classes.

2.5.5.2. Maternal measures and variables

Several demographic and previously utilised prenatal variables were included in this analysis: the mother's age at delivery, socioeconomic status (SES), neighbourhood quality, the presence of a partner, maternal childhood home disruption, and maternal childhood sexual abuse (see Section 2.5.1.). In controlling for the influence of the postnatal period, multiple maternal variables were chosen concerning postnatal psychopathology (postnatal anxiety, somatic symptoms, and depression), and general attitudes on parenting (maternal enjoyment and maternal confidence). Adverse life events from the post-natal period (child's birth through age 6 years) were also utilised.

A variable describing the relationship of the mother's parents was incorporated in this analysis as a life event. A series of 8 items exploring their parental relationship was asked in the questionnaire 'Your Health, Events, and Feelings' (34 months postnatal), phrased in Likert type format, and scored from 1-4 ('yes, always', 'yes, frequently', 'yes, sometimes', and 'not at all'; single parents were coded as missing). During ALSPAC data coding (Cripps et al., 2017), items 1, 3, 5, and 8 were recoded as (1=0, 2=1, 3=2, 4=3) and items 2, 4, 6, and 7 were recoded as (1=3, 2=2, 3=1, 4=0). Items were then summed to produce the sub-score, ranging from 0-21, and was coded and used as a continuous variable.

1. How would you describe the relationship between your mother and father when you were growing up? When together were they violent?
2. …affectionate?
3. …quarrelsome?
4. …happy?
5. …frightening?
6. …friendly?
7. …respectful of one another?
8. …remote or dismal from one another?

A 7-item scale describing the mother's home dwelling situation was asked at 32 weeks gestation ('About Yourself', The ALSPAC Study Team, 2009b). The below items were phrased as binary (1='yes', 2='no') and during ALSPAC data coding, were coded as a binary variable. Items 4 and 5 listed multiple options and those bolded were as part of this phase. For use in this analysis, item 7 was dropped and items 1-6 were recoded as (2=0, 1=1), summed, and the resultant variable recoded as (0=0, 1-6=1) to produce an aggregate variable describing home displacement. Home displacement was coded and used as a binary variable.

1. Were you legally adopted?
2. Were you ever "in care" of either a local authority or voluntary agency e.g. Bernardos?
3. Did your parents divorce or separate before your 18th birthday?

4. Did you ever live away from home with any of the following before you were 18 years old?
    a. Grandparents
    b. Other relatives
    c. Friends
    d. Foster parents
    e. Other (please describe)
5. Did you ever stay away from home in any of the following places before you were 18 years old?
    a. Hospital
    b. Boarding school
    c. Children's home
    d. Hostel
    e. In custody detention centre
    f. Other (please describe)
6. Did you leave home before your 18th birthday?
7. At each of the time periods given (0-5 years, 6-11 years, 12-16 years), during your childhood, who of the following lived in your home (other than for holidays or short visits)?
    a. Mother
    b. Father
    c. Brother(s)
    d. Sister(s)
    e. Step-mother
    f. Step-father
    g. Step-brother(s)
    h. Step-sister(s)
    i. Mother's partner
    j. Father's partner
    k. Grandmother
    l. Grandfather
    m. Family friend
    n. Other (please describe)

Psychopathology measures included the 3 sub-scores of the Crown-Crisp Experiential Index (CCEI; Crown & Crisp, 1966, 1970); anxiety, somatic symptoms, and depression. The CCEI has been found to have high validity as a measurement scale for the factors described (Alderman, Mackay, Lucas, Spry, & Bell, 1983), with the inclusion of somatic symptoms cited as valuable (Bramley, Easton, Morley, & Snaith, 1988). Further, the factors were found to correlate with the extraversion-neuroticism scale (Sam & Manickam, 1996), with a high degree of clinical reliability (Birtchnell, Evans, & Kennard, 1988).

This measure, comprising of 23 items, was given 4 times during the postnatal period in the maternal self-complete questionnaires 'Me and My Baby ' (8 weeks postnatal, 'Looking After the Baby' (8 months), 'Caring for a Toddler' (22 months), and 'Your Health, Events, and Feelings' (34 months). For ALSPAC use, the CCEI was modified from binary responses (yes/no) and 3-point Likert type items to 4-point Likert type items for consistency (The ALSPAC Study Team, 2009a) and scored from 1-4 ('very often', 'often', 'not very often', and 'never').

While there are no clinical thresholds built into the CCEI, a study of scores between all-female community and clinical populations (N=208, N=40, respectively), found a clinical range in CCEI total score of 40-52 (Birtchnell, Evans, & Kennard, 1988) out of a total 74, or an upper 45%. This range was also suggested by Joukamaa (1992), though validation in clinical populations was suggested. Elliott et al. (2000) found an upper 45% mean for the depression sub-score in a clinical population, and it was decided to apply that threshold in coding here. The anxiety and depression sub-scores at each time point were recoded to (0-8=0, 9-16=1) and the somatic symptoms sub-scores at each time point were recoded to (0-7=0, 8-14=1). The 4 time point scores for each domain were then summed and recoded to (0=0, 1-4=1) to produce an aggregate variable for postnatal anxiety, somatic symptoms, and depression from 8 weeks to 34 months.

The anxiety sub-score was based on the below items. During ALSPAC data coding (The ALSPAC Study Team, 2009a) items 1, 3, and 4 were recoded to (1,2=2; 3,4=0), items 5, 6, 7, and 8 were recoded to (1,2=2; 3=1; 4=0), and item 2 was recoded to (1,2,3=2; 4=0). Items were summed to produce the sub-score with a range

of 0-16, coded by ALSPAC as a continuous variable, and recoded to a binary variable as above.

1. Do you feel upset for no obvious reason?
2. Do you sometimes feel panicky?
3. Do you feel strung-up inside?
4. Do you ever have the feeling you are going to pieces?
5. Have you felt as though you might faint?
6. Do you feel uneasy and restless?
7. Do you worry a lot?
8. Do you have bad dreams which upset you when you wake up?

The somatic sub-score was based on the below items. During ALSPAC data coding (The ALSPAC Study Team, 2009a), items 1, 2, and 3 were recoded as (1,2=2; 3=1; 4=0), items 4, 5, and 6 were recoded as (1,2=2; 3,4=0), and item 7 was recoded as (1,2=0; 3,4=2). Items were summed to produce the sub-score with a range of 0-14, coded by ALSPAC as a continuous variable, and recoded to a binary variable as above.

1. Do you get troubled by dizziness or shortness of breath?
2. Do you feel tingling or prickling sensations in your body, arms or legs?
3. Do you feel tired or exhausted?
4. Do you feel sick or have indigestion?
5. Do you find that you have little or no appetite?
6. Do you often have excessive sweating or fluttering of the heart?
7. Can you get off to sleep alright?

The depression sub-score was based on the below items. During ALSPAC data coding (The ALSPAC Study Team, 2009a), items 1, 2, 3, and 4 were recoded as (1,2=2; 3=1, 4=0), items 5, 6, and 7 were recoded as (1,2=2; 3,4=0), and item 8 was recoded as (1,2=0; 3,4=2). Items were summed to produce the sub-score with a range of 0-16, coded by ALSPAC as a continuous variable, and recoded to a binary variable as above.

1. Do you feel that life is too much effort?
2. Do you experience long periods of sadness?
3. Do you find yourself needing to cry?
4. Do you have to make a special effort to face up to a crisis or difficulty?
5. Do you regret much of your past behaviour?
6. Do you wake unusually early in the morning?
7. Do you lose the ability to feel sympathy for others?
8. Can you think quickly?

A scale measuring the respondent's attitudes on parenting was included in this analysis. Developed and piloted by the ELSPAC team (Taylor, Golding, & Bishop, 1996), it was given in the questionnaires 'Looking After the Baby' (8 months) and 'Your Health, Events, and Feelings' (34 months). This measure consisted of 11 items and 2 sub-scores, maternal enjoyment and maternal confidence. Items were phrased in Likert type format and scored 1-4 ('exactly feel', 'often feel', 'sometimes feel', and 'never feel'). As used in this analysis, the maternal enjoyment and maternal confidence sub-scores at the 2 time points were summed to produce aggregate continuous variables ranging from 0-33, representing these constructs throughout the postnatal period.

The maternal enjoyment sub-score was based on the below items. During ALSPAC data coding (Taylor, Golding, & Bishop, 1996; Cripps et al., 2017), items 1, 2, 4, and 5 were recoded as (1=3, 2=2, 3=1, 4=0) and item 3 was recoded as (1=0, 2=1, 3=2, 4=3). Items were then summed to produce the sub-score, ranging from 0-15, and was coded and used as a continuous variable as above.

1. I really enjoy my baby.
2. It is a great pleasure to watch my baby develop.
3. I feel I should be enjoying my baby but am not.
4. Having a baby has made me feel more fulfilled.
5. Babies are fun.

The maternal confidence sub-score was based on the below items. During ALSPAC data coding (Taylor, Golding, & Bishop, 1996; Cripps et al., 2017), items 1, 3, 4, 5, and 6 were recoded as (1=0, 2=1, 3=2, 4=3) and item 2 was recoded as (1=3, 2=2, 3=1, 4=0). Items were then summed to produce the sub-score, ranging from 0-18, and was coded and used as a continuous variable as above.

1. I would have preferred that we had not had this baby when we did.
2. I feel confident with my baby.
3. I dislike the mess that surrounds my baby.
4. I really cannot bear it when the baby cries.
5. I feel constantly unsure if I'm doing the right thing for my baby.
6. I feel I have no time to myself.

During ALSPAC data coding, the maternal enjoyment and maternal confidence sub-scores were then summed to produce the maternal bonding score, ranging from 0-33, which was coded as a continuous variable, but which was not utilised in this analysis.

Instances of domestic violence were also used as part of this analysis. A section of the questionnaire ‘Mother and Family’ (8 years) included a section covering the partner relationship in the form of a 48-item scale (The ALSPAC Study Team, 2007a). Two items from this scale were used, domestic violence committed by the mother against the partner and domestic violence committed by the partner against the mother. These items were phrased in Likert type format, scored from 1-3 (‘no’, ‘yes, sometimes’, and ‘yes, often’) and during ALSPAC data coding, were coded as a categorical variable (The ALSPAC Study Team, 2007a). For use in this analysis, both variables were recoded as (1=0, 2=1, 3=1) and summed, with the resultant variable recoded as (0=0, 1=1, 2=1) and used as binary variable representative of domestic violence regardless of offender/victim role.

A measure exploring life events was given in the questionnaires ‘Me and My Baby’ (8 weeks postnatal), ‘Looking After the Baby’ (8 months), ‘Caring for a Toddler’ (22 months), ‘Your Health, Events, and Feelings’ (34 months), and ‘Mother’s New Questionnaire’ (4 years) consisting of 42 items describing major and

adverse life events (see Appendix D) presented in Likert type format, scored from 1-5 (‘yes, affected me a lot’, ‘yes, moderately affected me’, ‘yes, mildly affected me’, ‘yes, but did not affect me’, and ‘did not happen’). A further item queried any other major event not listed (text entry) but did not contribute to the aggregate score. During ALSPAC data coding (The ALSPAC Study Team, 2009), items were recoded as (1,2,3,4=1; 5=0). Items were then summed to produce the sub-score which was coded and used as a continuous variable.

2.5.5.3. Child measures and variables

Child data used in Chapter 7 were child’s gender and experience of adverse life events from birth to age 8.5 years. Both variables were used as discussed above in Section 2.5.3.1.

2.6. Data Collection

To ensure the reliability and validity of study data, ALSPAC used several different collection methods. Inconsistent methods can skew results or invalidate studies, so the design of ELSPAC studies stressed standardisation across branch projects and within specific projects (Golding, 1989). In-person clinic visits with the mothers (both pre- and postnatal) and with the study children allowed for biometric and biological sample collection in a standard clinical setting. Questionnaires provided the bulk of the data, ensuring an accurate picture of every facet of the study child’s life through the eyes of their mother/primary caretaker, teachers, and themselves. Lastly, in-home observation and environmental monitoring caught valuable information on the study family’s environment that they might not be aware of. The intensity of ALSPAC data collection effectively ‘left no stone unturned’ in terms of potential contributory factors to the study child’s health outcomes.

2.6.1. Physical data collection

Biological samples were collected from both the maternal and offspring cohorts at several stages during the first wave of study. Mothers who attended these clinics during the prenatal period provided consent for their blood (as whole blood, red cells, white cells, plasma, and serum) and urine to be collected (Fraser et al., 2013). Following delivery, cord blood, portions of umbilical cord, and the placenta were also collected, with hair and toenail clippings taken from the infants shortly after birth, as were milk teeth when they were naturally shed (age 4-5 aprox.; Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001). Blood collection occurred routinely for a small sub-sample (Children in Focus, CiF), at age 7-7.5 for the entire cohort, and then routinely from age 11 through 18, in addition to hair/nail clippings, urine, and saliva swabs (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001; Fraser et al., 2013). A data bank of maternal DNA was established with the intention of creating genome-wide assays and methylation analyses, both individual and in mother-child pairs where child DNA is also available. Complete genome and methylome sequencing were planned for the child cohort and are underway, with DNA sampling done for N=11,343 of the participants (see Boyd et al., 2012 and Fraser et al., 2013 for complete genetic analysis methodologies).

Biometric data were also collected from both cohorts. For the mothers, this entailed prenatal clinic visits featuring physical examination and the above biological sample collection. For the CiF child sub-sample, collection occurred during the routine clinic visits and involved a detailed interview and physical examination. Physical demographics were taken at this time (height, weight, body circumference measurements, blood pressure, speech, teeth and skin inspection) in addition to testing (cognitive functioning, sight/hearing, lung functioning, allergens), evaluation (diet, fitness, parental interview), and screening as part of prevalence studies (physical developmental problems, cognitive developmental issues, anaemia, and otitis media) (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001).

2.6.2. Questionnaires

The bulk of ALSPAC data were collected via questionnaires distributed at regular intervals in two categories; self-completion by the mother, partner, or child with themselves as the subject, and child-based, completed by the mother/carer, and teacher/primary educator with the study child as the subject. Involvement of the partner was done solely at the discretion of the mother, as any survey for the partner was sent along with the corresponding survey for the mother, addressed to her, with instructions that inclusion of the partner in the study was her decision (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001).

The maternal self-completion questionnaires began at 8 weeks gestation and continued through 12 years, 1 month. A further questionnaire on adult learning was sent out in 2004, and a further 2 in 2010 covering general life and health (Table 2.1). These questionnaires covered a variety of topics including demographics, the mother's medical history, psychiatric/substance abuse history, family history, eating habits, household exposures (including mean temperature), socioeconomic status, major life events, pregnancy attitudes and outlook, and social relationships (see Appendix A for a complete inventory of maternal questionnaires/surveys). Self-completion questionnaires for the partner began at 8 weeks gestation and mirrored the mother series schedule with the exception of 32 weeks gestation and 8 weeks postnatal. In addition, the partner also received the 2004 adult learning questionnaire and the general life/health questionnaires in 2010 (Table 2.3). The partner series was similar to the mother series, focusing on the same variables and demographic information. Self-completion questionnaires for the study child began at age 5 years, 5 months with a series of 6 questionnaires over 2 years, continuing roughly every 6 months until age 11, when multiple questionnaires were sent per year. As the study child entered adulthood, the questionnaires normalised to a one-per-year schedule, which continued to follow them as they transitioned to adulthood and is currently running.

Table 2.3. ALSPAC self-complete questionnaire schedule

Study Child Age	Mother	Partner	Child
8 weeks gest.	X	X	
12 weeks gest.	X	X	
18 weeks gest.	X	X	
32 weeks gest.	X		
8 weeks	X		
8 months	X	X	
21 months	X	X	
33 months	X	X	
47 months	X	X	
5 years, 1 month	X	X	X
5 years, 5 months			X
6 years, 1 month	X	X	X
6 years, 5 months			X
6 years, 9 months			X
7 years, 1 month	X	X	X
7 years, 7 months			X
8 years, 1 month	X	X	X
8 years, 7 months			X
9 years, 2 months	X	X	X
9 years, 8 months			X
10 years, 2 months	X	X	X
10 years, 8 months			X
11 years			multiple
11 years, 2 months	X	X	
12 years			X
12 years, 1 month	X	X	
13 years			multiple
14 years			X
15 years, 6 months			X
16 years			X
17 years, 6 months			X
18 years			multiple
19 years, 6 months			X
20+ years			X
21+ years			X
22+ years			X
23+ years			X
2004	X	X	
2010	X	X	

The mother/primary caretaker completed most of the child-based questionnaires, with the study child's teacher completing a series of 5 school-based questionnaires at school years 3, 4, 6, and 8, covering the child's academic performance, proficiencies/deficits, and socialisation. The series completed by the mother involved 24 separate questionnaires beginning at ages 4 weeks through 16 years (Table 2.4). A series of 9 questionnaires on puberty began at 8 years, 1 month and continued through 17 years, completed by both the mother and child (Table 2.3). These surveys covered health, psychopathology, exposure, life events, socialisation, and a variety of environmental variables (see Appendix B for a complete inventory of child-completed questionnaires/surveys). With questionnaires completed by children, extra care was taken by ALSPAC to accurately code the data received. Special instructions were given to coders specifying i) only ticks, numbers, or text was counted for questions of tick, number, or text type responses, ii) blank answers or entries struck out by the respondent were counted as blank and, iii) improper type responses and written 'don't know' responses were coded as missing (The ALSPAC Study Team, 2009). Coding protocol (both ALSPAC general coding protocol and survey-specific protocol) was laid out in a separate document and all coding was given a second check by the primary coder before undergoing a check by a member of the ALSPAC study staff (The ALSPAC Study Team, 2009).

Table 2.4. ALSPAC child-based questionnaire schedule

Child Age	Mother	Educator	Child
4 weeks	X		
6 months	X		
15 months	X		
18 months	X		
24 months	X		
30 months	X		
38 months	X		
42 months	X		
54 months	X		
57 months	X		
64 months	X		
69 months	X		
78 months	X		
81 months	X		
91 months	X	X	
97 months*	X		X
103 months	X	X	
9 years	X		
9 years, 7 months*	X		X
10 years	X	X	
10 years, 8 months*	X		X
11 years	X		
11 years, 8 months*	X		X
13 years	X	X	
13 years, 1 month*	X		X
14 years, 7 months*	X		X
15 years, 6 months*	X		X
16 years	X		
16 years*	X		X
17 years*	X		X

2.6.3. In-home environmental monitoring

Smaller sub-samples have had environmental monitoring taking place within the home. Studied variables included air pollutants (over 1 year in N=170 homes), nitrogen oxides (over 2 weeks in N=1200 homes), carbon monoxide (over 5 days in N=80 homes with inhabitant blood carboxyhaemoglobin comparisons), noise

pollution (N=80 homes), nursery temperature (over 1 year in N=2000 homes), and magnetic radiation from home electronic proximity (N=50 homes) (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001).

2.6.4. Health and education records

With the permission of the mother, ALSPAC was able to access all prenatal medical records and any involving the study child. Participating women were given detailed information on the use of their medical data as a member of the ALSPAC maternal cohort and advised of their right to opt out at any time (Fraser et al., 2013). Obstetric records were first manually abstracted only in certain cases (caesarean birth, tool-assisted birth, or various studies) but grants have since made abstraction possible for the full cohort. Manually abstracted data were transferred to an electronic system and presently, all abstraction is done electronically (Fraser et al., 2013). In addition, ALSPAC participant mothers are flagged (with permission) in the NHS Central Register for all-cause mortality, cancer, and emigration and child cohort has been linked the NHS registries for death and cancer (Boyd et al., 2012). As part of an initiative combatting missing data from inactive/partially active members of the child cohort, efforts have been made to perform routine data collection on these members through a health records link. PEARL (the Project to Enhance ALSPAC through Record Linkage; Boyd et al., 2012) is planned for use in data linkage and collection for eligible non-participants to assess attrition and participation bias. (Boyd et al., 2012; 2019).

As the child cohort was spread across 3 school years, educational data linkage was important. Approximately 82% of the ALSPAC eligible sample had educational records linked from the National Pupil Database (Boyd et al., 2012). School entry exams and national testing records were linked to the database, with most schools able to provide Key Stage assessment and school census data.

2.7. Data Use Permissions and Ethics

In compliance with the terms of use (ALSPAC Executive Committee, 2020), this project lodged a proposal for data use with the University of Bristol. This proposal detailed the research topic and a complete literature review in support of the research goals, as well as an outline of proposed analyses. After review and acceptance by the designated associate from ALSPAC, a catalogue of variables was requested, and research funds were made available to cover ALSPAC data fees. Before data were exchanged, an agreement of ethical use and protection of the ALSPAC data (see Appendix C) was signed. Throughout this investigation, all data was handled as specified in this agreement and in compliance with the ethical research terms of Ulster University (Ulster University, 2019).

2.8. On-Going Research

To date, ALSPAC continues to collect data on the original cohort, Children of the 90's (University of Bristol, 2020e) and has moved into research with the next generation, Children of the Children of the 90s (COCO90s; University of Bristol, 2020a). Information on health initiatives and new research is disseminated via the ALSPAC webpage, hosted on the University of Bristol's webpage, a dedicated Twitter account, and YouTube channel (University of Bristol, 2020f). As of October 2019, continued collaboration between the University of Bristol, the MRC, and the Wellcome Trust has resulted in additional funding for the next 5 years of the project (University of Bristol, 2019).

2.9. Language Use

It is in the nature of animal research to use the term 'offspring' and many of the non-human studies referenced here have done so. It is in human nature to use the term 'child' when referring to offspring. This work utilised these terms interchangeably to avoid semantic saturation but also because humans are animals, albeit very successful ones. This language choice was reflective of the work and was

not meant to imply anything about the population cohorts, nor to dehumanise or cause offence to any of the participants. Finally, as maternal respondents provided their gender identity as ‘female’ at the time of data collection, gendered language has been used throughout.

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Chapter 3

Modelling the prenatal maternal social environment

3.1. Study Introduction

The previous chapter laid out the main theories and influences behind the undertaking of this thesis, the hypothesis it was intended to test, and the collection methodologies of the study data used to test it. As this project followed a temporal flow, analyses were performed following the timeline of ALSPAC's first wave from 8 weeks gestation in the maternal cohort through the offspring cohort's adolescence. The first step in this process of examining if the prenatal maternal social environment affected the psychopathology of offspring was to operationalise that environment in order that it might be tested. This process involved reviewing the prenatal data and selecting variables to use in creating and testing a statistical model of the prenatal maternal social environment. As this first analysis would be the foundation for all pursuant analyses and the literal rock on which this thesis was built, the data used had to be of high contextual value.

Data use decisions were driven by the literature underlying the main hypothesis. While the simplest method available in testing this was the DNA, genome, and methylation data, the presence of an epigenetic modification would not indicate behaviour, the presence of distress, or the experience of psychopathology in the offspring cohort. Nor would the lived experience of socialisation or isolation be present in the maternal genomic data. It was decided that the main hypothesis of this thesis should be tested via quantitative means first, with the option to examine genomic data in a follow-up study if successful. To that end, a bank of variables from both cohorts were selected that best covered the concepts and environments to be explored over several phases of analysis. For this phase, an exploratory factor analysis (EFA) modelling the underlying structure of the prenatal maternal social environment, a scale was selected detailing participants' social network and expectations of social support.

This scale's items covered quantity of friends and interactions, social interactions directly related to the pregnancy, the intimacy of relationships, and the types of social and monetary support the participants expected and from whom. The dual sub-scales of this metric mirrored the 2 main spheres of influence hypothesised of the prenatal maternal social environment: the effect of socialisation or isolation on

the mother and, the effect of maternal socialisation or isolation on the offspring. This psychosocial data (including the social scale used in this chapter) provided insights into the mother's relationship with the prenatal maternal social environment and data was acquired to test the eventual psychopathologic outcomes for the offspring in potential mismatch adolescent social environments. Explaining the relationship between the prenatal maternal social environment and these offspring outcomes involved exposing the likely mechanics of that relationship. The literature detailing biological prenatal reactions to maternal stress/distress and the importance of socialisation, both developmentally and overall, was fertile ground for these investigations.

3.1.1 Prenatal epigenetics in humans

Every human is an heir to all preceding environments but the more distal the environment, the lesser the impact on the individual (Rushton, Russell, & Wells, 1984; Repetti, 1987; Rushton, 1988). The first environment with a direct proximal effect on a person is *in-utero*, a micro-environment existing within the mother, who is herself the centre of concentric, nested environments (Bronfenbrenner, 1979). ALSPAC prenatal data collection left no maternal environment unturned, understanding the importance of foetal developmental period and focusing on any and every variable which could affect it (Prokhorskas, Ignatyeva, Dragonas, & Golding, 1989; Golding et al., 2001; 2004; Boyd et al., 2012). This raw data covered everything from the average temperature of the mother's sitting room to the products she came into contact with, food and drink, present and past emotional states, to every facet of her demographics. Thus, the prenatal data constituted a rich resource of the pregnancy by casting a wide net and catching as many potentially vital variables and confounders as possible. While an exhaustively thorough undertaking, it meant a full array of information on anything with a possible prenatal epigenetic impact.

The members of the ALSPAC maternal cohort were being considered in a similar context to a hypothetical prehistoric woman alone in the wilderness, pregnant, and forced to fend for herself. With no guarantee of companionship, the

safety of a group, or even anyone to guard against predators as she slept, her environment was hostile. Chances of survival were slim but even stripped of the vital protections of her kin, there was a final safety-net for her child. The interaction between this woman and her environment could inform changes in her own genome (Jaenisch & Bird, 2003; Meaney, 2010; Carey, 2012) and that of her child (Barker, 1997; Heijmans et al., 2008; Soubry, Hoyo, Jirtle, & Murphy, 2014). This epigenetic process, methylation switching genes on/off to produce phenotypic expressions during the lifespan (Miner, Sultan, Morgan, Padilla, & Relyea, 2005; Feinberg, 2007) which are heritable (Carey, 2012; Yehuda et al., 2016), is well established in the literature. Environmental pressures are perceived by the mother's body and communicated to the foetus chemically via maternal hormones through the placenta (Haig, 1996; Griffiths & Campbell, 2015), where the genome can react to this information. Epigenetic modifications during pregnancy can be seen as emergency 'stopgap' measures designed to give the foetus whatever bonus to survival chance exists, no matter how small.

The nature of these changes depends in part on the nature of the hostile environmental pressures. Non-human mammal studies have shown type-dependent modifications in the offspring of prenatally stressed mothers, including altered spatial development in the offspring of overcrowded rats (Hayashi, Nagaoka, Yamada, Ichitani, Miake, & Okado, 1998), increased cortisol response in the offspring of unpredictable-noise-stressed Rhesus monkeys (Clarke, Wittwer, Abbott, & Schneider, 1994), and heightened open space anxiety in the offspring of light/noise stressed rats (Weinstock, Matlina, Maor, Rosen, & McEwen, 1992). Social isolation has been used as a prenatal stressor in rat models (see Gudsnuk & Champagne, 2012 for review) but the body of literature concerning isolation as a prenatal stressor in humans is small (Kaiser & Sachser, 2009). It has been theorised that humans are as susceptible to type-dependent modifications as non-human mammals, with physiological findings from the Dutch Famine Study (Roseboom, de Rooji, & Painter, 2006) and in the descendants of Holocaust survivors (Yehuda et al., 2016). If the prenatal maternal social environment can influence offspring behaviour in animals (Gudsnuk & Champagne, 2012), and if these behaviours constitute a type-dependent adaptation, and if humans can show type-dependent adaptations to the prenatal maternal social environment, it was hypothesised that the

prenatal maternal social environment of the ALSPAC maternal cohort could affect behaviour in the offspring cohort as a functional adaptation to conditions of the prenatal maternal social environment.

Cortisol's ability to cross the placental barrier created the potential for maternal stress to affect the foetal genome (Hompes et al., 2013; Richards, Woods, Rabaglino, Antolic, & Keller-Wood, 2014), regardless of the mother's perception of the stressor, which here was low socialisation/isolation. Laplante, Brunet, Schmitz, Ciampi, and King (2008) found both objective stress and subjective experience of stress related to lower cognitive and language abilities in young children who were *in utero* during the Québec ice storm of 1998. Project Ice Storm, a longitudinal study of the prenatal maternal stress resultant of the storm, measured both the subjective experience of stress and objective exposure to the stressor. Bush et al. (2017) measured both objective stressful life events (SLE) and perceived stress (PS) during the prenatal period in a low-income sample and found both associated with negative infant temperament and stress recovery. Even if the mother does not perceive a harsh environment as stressful, her body will, triggering automatic processes to increase survival odds for the foetus. While this may seem unsettling for the individual, it points to the potential for universality, i.e., this is an environmentally dependant protocol that will occur for any pregnant woman rather than an emotionally driven process occurring in a subset of women.

Human prenatal stress studies differ from animal studies as causing distress to expectant mothers constitutes a violation of professional ethics. Thus, these studies rely on opportunistic stressors (crisis, war, natural disaster) or are prospective studies utilising pre-existing personal stressors and/or pregnancy-specific stressors. Such studies can be singular, examining prenatal stress and its relationship with a specific variable or health outcome, or part of a larger longitudinal design with health and mental health outcomes monitored throughout development, into adulthood, and potentially into the next generation. ALSPAC is an example of one such generational study and its main aim since inception has been studying environmental effects from pregnancy through adulthood (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001; Golding & the ALSPAC Study Team, 2004). Additionally, collection and analysis of genetic samples has become less difficult

and expensive, allowing for genome-wide association studies (GWAS) to assess traits in large populations, and for anonymised databases of population-level genetic data. Thus, research can be association-based, correlating prenatal stress (subjective or objective) with an offspring outcome, examine specific genotypic variance, or employ mixed methodology. This project was association-based, examining maternal socialisation and its relationship with offspring psychopathology.

3.1.2. Socialisation in humans

Humans are a social species and proper human brain development depends on socialisation (Johnson, Grossman, & Kadosh, 2009; Frenkel & Fox, 2015), to the extent that infants are capable of facial mimicry within the first 1-2 weeks of life (Lavelli & Fogel, 2002). Infants raised with low social contact can suffer from a variety of physical and mental problems, including delayed/impaired development (Carlson & Earls, 1999), poor cognitive functioning (Mills et al., 2010), social cognition (Azar, McGuier, Miller, Hernandez-Mekonnen, & Johnson, 2017), and impaired psychosocial behaviour (Strathearn, 2011). Lack of social connectivity also constitutes a significant risk factor in all-cause mortality (House, Landis, & Umberson, 1988; Holt-Lunstad, Smith, & Layton, 2010). Most notable is Reactive Attachment Disorder (RAD), in which the child develops a disturbed base 'template' for social interactions and relationships due to severe abuse and/or neglect in early life, and are highly reactive to environmental changes, exhibiting maladaptive behaviour (World Health Organisation, 2004). Children raised in neglect during the crucial period of language development can also experience language deficit, impairments which are difficult to overcome once the developmental period has passed (Allen & Oliver, 1982; Spratt et al., 2012). Total isolation during the language development phase can produce 'feral' children who may never fully acquire language (Fromkin, Krashen, Curtiss, Rigler, & Rigler, 1974; Curtiss, Fromkin, & Krashen, 1978). Socialisation and group living were primate traits which yielded species success to the extent that these traits were inexorably entwined with the evolution of the modern *Homo Sapiens* brain (Frith & Frith, 2010). The importance of socialisation to humanity was eloquently summarised in Cacioppo and

Patrick (2008): "*Once again, the social and the physiological cannot be separated any more than we can separate the length from the width of a rectangle*."

Socialisation's importance in brain development and wellbeing changes as the individual ages. Infancy/early childhood socialisation is vital for foundational brain development, as brain plasticity allows for social interactions to literally change brain physiology (Curley, Jensen, Mashoodh, & Champagne, 2010). In later childhood/adolescence, socialisation aids adaptive socio-cognitive development and the understanding of an individual as themselves in the wider context of others. This developmental phase includes significant brain growth and maturation of the medial prefrontal cortex, which governs social judgement, cognition, and self/other perspective evaluation (Mitchell, Banaji, & Macrae, 2005; D'Argembeau et al., 2007; Denny, Kober, Wager, & Ochsner, 2012). An adult is considered 'cognitively mature' at approximately age 25, but though brain development is complete, the brain is not static. In adulthood, socialisation maintains an individual's 'social homeostasis', a balance between loneliness and over-saturation with abject isolation functioning as a deficit environment (Matthews & Tye, 2019). Finally, during the geriatric years, socialisation provides valuable stimuli which protects against cognitive degeneration (Blazer, 1982; Bassuk, Glass, & Berkman, 1999), true for face-to-face interactions and technology-assisted socialisation (Tsai, Tsai, Wang, Chang, & Chu, 2010). Geriatric socialisation is also fulfilling for the individual and is important to maintaining both physical and mental wellbeing (Lee & Ishii-Kuntz, 1987; Wang, 2014).

Insufficient socialisation (isolation) causes significant issues at any age. While more primitive issues of isolation are now irrelevant (predator protection) or subsumed by the state/society in many regions (care during illness, infirmity, or old age; access to shelter, food, and physical means if destitute), some persist. Isolation, whether abject or relative, deprives the brain of social stimuli and can lead to profound neurological and psychological consequences. These impairments include executive functioning (Cacioppo & Cacioppo, 2014), cognition, and social cognition (Cacioppo & Hawkley, 2009), as well as increased risk for all-cause morbidity and mortality (Cacioppo, Capitanio, & Cacioppo, 2014). Psychologically, social isolation can lead to depressive symptomology (Alpass & Neville, 2003; Taylor, Taylor,

Nguyen, & Chatters, 2018), mood and anxiety disorders (Chou, Liang, & Sareen, 2011), and increased risk of psychosis (Broome et al., 2005; Reininghaus et al., 2008). Loneliness can be considered the emotional fallout of isolation, a state born of both deficit and profound need. If isolation is famine then loneliness is hunger, a call to action by the body to fill the need and return to homeostasis. Anyone can experience isolation and loneliness at any point in the lifespan, from a neglected infant to a bullied child and from a loner adult to a forgotten elderly individual. Taken in this context, socialisation is as important to mental and physical wellbeing of the expectant mother as it will be for her offspring.

At this stage it is important to mention that there is no 'normal' amount of socialisation, rather there is an 'optimal' amount of socialisation for each individual. It is a fluid environment in which one exists, and is dependent on several factors, particularly individual differences (Fishman, Ng, & Bellugi, 2011). Cacciopo and Patrick (2008) discussed this in terms of an internal social 'thermostat', or a level of socialisation that maintains individual homeostasis. Where a 'social butterfly' thrives in and prefers highly social environments, others feel more comfortable in the occasional company of a few close confidants, and there are individuals who seek the calm of solitude over most social situations. All of these levels of socialisation are right for the individual, who may self-select if given the choice (Hills & Argyle, 2001) or feel distress if in a social environment that is a 'mismatch' to what they prefer (Geen, 1984). To follow the metaphor of the internal social 'thermostat', what determines its setting?

The answer is internal, its root in the relationship between social contact and the central nervous system (CNS). A human being confronted with sensory input enters a state of arousal, a physiological readiness and responsiveness to stimulation. Being suddenly confronted by an aggressive dog and meeting a playful puppy both result in arousal, though with radically different catalysts and CNS outcomes. Humans are also capable of generating internal arousal without the need for external stimuli, for example, by listening to an upbeat song or rehashing a terrifying memory. Social contact generates arousal in the CNS allowing for increased reactivity to input, ability for reactive motion, and emotional sensitivity (Pfaff, Ribeiro, Matthews, & Kow, 2008). Individuals vary in terms of internal arousal and

need for external arousal, and this premise forms the core of extraversion personality theory (Eysenck, 1975, 1967, 1983), which describes an individual's internal and external behaviours as they relate to arousal and modulation of that arousal (Eysenck & Eysenck, 1985). It is suggested that those with high internal arousal will seek less from external sources (introversion) and those with low internal arousal will seek more (extraversion). Physiological arousal can be measured and visualised by various brain imaging techniques and physiological measuring, leading to extensive research into extraversion personality theory (EEG: Matthews & Amelang, 1993; Beauducel, Brocke, & Leue, 2006, MRI/fMRI: Hagemann, Hewig, Walter, Schankin, Danner, & Naumann, 2009; Kehoe, Toomey, Balsters, & Bokde, 2011, PET: Fischer, Wik, & Fredrikson, 1997). Personal arousal homeostasis could be considered as the social 'thermostat' setting, with an individual moderating their socialisation (and thus their social environment) to fit within their comfort zone of homeostasis. A biological model of this process exists, explaining the mechanisms behind it.

The process of CNS activation to desired homeostasis through social moderation and other social behaviours have their origin in genetic inheritance, the environment, and interaction between them (Knafo & Plomin, 2006; Ebstein, Israel, Chew, Zhong, & Knafo, 2010). The role of genetics in behaviour (behavioural genetics) has been well established and is central to biopsychosocial theories of personality psychology, as extraversion is highly heritable. A meta-analysis of 62 studies examining heritability in extraversion found a mean effect size of 40% of the variance in extraversion due to genetics (Vukasović & Bratko, 2015) while twin studies have found heritability estimates as high as 54% (Jang, Livesley, & Vernon, 1996) and ranging from 23% to 45% in adult twins reared apart (Pedersen, Plomin, McClearn, & Friberg, 1988). The extraversion spectrum describes an individual's relationship with internal and external arousal, social behaviours that regulate that arousal, and genetic variance contributing to their optimum levels for homeostasis; the social 'thermostat'.

Additionally, the genetic component of extraversion suggests the potential for epigenetic modifications which could impact behaviour. Puglia, Lillard, Morris, and Connelly (2015) found that methylation of the oxytocin receptor gene (*OXTR*)

affected fear response with implications for social cognition. In cognitive studies, individuals high in extraversion showed less social anxiety (Blumenthal, Chapman, & Muse, 1995) though were more readily distracted (Blumenthal, 2000) due to differences in arousal. As an 'extravert' would seek arousal to reach homeostasis, an 'introvert' has higher internal arousal, which can be observed by neuroimaging and biometric monitoring (Canli, 2004). Prenatal research had shown an association between maternal cortisol due to distress and infant reactivity (Werner et al., 2013) and infant temperament (Buitelaar, Huizink, Mulder, de Medina, & Visser, 2003; Werner et al., 2007); both of which can be used as indicators of arousal (Blair et al., 2008). Increased internal arousal is indicative of increased CNS reactivity to stimuli, a state of increased preparedness for reaction, which has obvious survival benefits. These are valuable behaviours in a crisis but maladaptive in a normative setting.

Taken together, 'optimal' socialisation is representative of an internal biological process varying by individual difference with a strong genetic facet, and phenotypic expression of those genes can be modified by epigenetic processes driven by environmental interaction with adaptive/maladaptive implications. If the prenatal maternal social environment environment resulted in offspring with high or low optimal socialisation, these offspring would be in environmental mismatch if they encountered a social environment contrary to their preferred level of socialisation. An individual's social environment can change over time and due to a multitude of factors, but children lack the social mobility of adults and thus see less change during childhood and adolescence. Therefore, an environmental mismatch may not have been a transient experience and exhibiting maladaptive behaviour could have meant significant distress for the individual.

In considering a broad evolutionary approach to the main hypothesis, an important aspect was that the ALSPAC data used was collected before the advent and popularisation of contemporary social media. The internet has existed in some form since the 1950s (Licklider, 1960; Licklider & Clark, 1962) and the first primitive social media platforms date from the 1970s (UseNet; Hendricks, 2013), however, the first instant messaging programs (ICQ, AOL Instant Messenger) and web-based social media platforms (bolt.com, sixdegrees.com) would not appear until the late 1990s (Hendricks, 2013). The data used to model the prenatal maternal

social environment was uncomplicated by the addition of technological social interaction, which could be considered a confounder in modern socialisation research. Socialisation here was face-to-face (as described by several items in the measurement scale) or the assumed long-distance proxies of telephone or letter. Low socialisation in this population constituted the legitimate objective stressor of isolation, an empirical representation of a lonely pregnancy.

3.1.3. Study aims

This thesis was undertaken to explore the potential epigenetic link between prenatal maternal socialisation, the foetal genome, and resultant environment-dependent outcomes. Testing the effect of an abstract concept like the prenatal maternal social environment on offspring psychopathology in adolescence meant showing that an abstraction had discreet outcomes. An untestable hypothesis is indistinguishable from a shower thought and just as fleeting, so the raw data had to be standardised and codified into an empirical model to facilitate testing. A scale measuring social networks and social support was given to the maternal cohort at 12 weeks gestation and this scale was used in an EFA to determine the prenatal maternal social environment's dimensional structure. An EFA was employed in the measurement model as it offered both contextual salience and statistical validity. These factors not only mathematically described the environment but were also contextual descriptors of the population's experience of and relationship with that environment.

The factors were also predicted to be meaningful epigenetically in defining not only the differences in socialisation in the maternal sample but also how those experiences impacted on foetal/child development. It was expected that isolation or a harsh social environment would constitute environmental pressure significant enough to act as a prenatal stressor, resulting in type-dependent adaptive epigenetic modifications. It was further predicted that while all dimensions would describe the prenatal maternal social environment, endorsement rates of these dimensions would vary among respondents, creating patterns of socialisation. Thus, the model identified in this analytical phase could then be used to stratify the maternal cohort

along the dimensions of the prenatal maternal social environment to describe socialisation in this population during pregnancy, making it possible for offspring to be considered as carrying a specific 'social phenotype'. Offspring in an adolescent social environment radically different from the prenatal maternal social environment, the environment they were 'primed' for, would be in environmental mismatch and subject to adaptive psychopathology. It was hypothesised that individuals primed for an isolation environment would fare better in that environment than those primed for a normative or highly social environment.

3.2. Methodology

3.2.1. Sample

The sample pool for this phase of the analysis consisted of all ALSPAC mothers in the initial gestation-recruitment wave of 1990-1991 (N=15,645) and cases with missing data were dropped (N=12,549). Mean age for this population was 27.77 years (SD=4.91 years) with a range of 15-45. Most respondents had an established history in the Avon catchment area; 53.4% had lived in/near Avon all their lives, 16.9% over 10 years, 11.2% between 5 and 9 years, 13.6% between 1 and 4 years, and 5% for under a year (Herrick, Golding, and the ALSPAC Study Team, 2008). The population was further described as 79.1% homeowners, 79.4% married, and 97.8% were white/Caucasian (Fraser et al., 2013).

3.2.2. Measures

The items for this model were taken from a larger, 20-item scale originally designed for use by ELSPAC (Prokhorskas, Ignatyeva, Dragonas, & Golding, 1989) and influenced by qualitative research undertaken by Thalia Dragonas in a cohort of Greek mothers (Dragonas, 1987; Thorpe, Dragonas, & Golding, 1992), as per Chapter 2 (Section 2.5.1). This scale appeared in the 'About Yourself' self-completion questionnaire given to the mothers at 12 weeks gestation. The exact wording of these items is quoted in Table 3.1.

3.2.3. Analytic strategy

An exploratory factor analysis (EFA) model was considered to simplify the data from item responses into more salient dimensions describing the maternal prenatal social environment. EFA is a technique used to determine the latent structure (i.e. unobserved structure) of a construct, in this case maternal socialisation, by analysing the relationships (i.e. correlations) between contributory variables. Integral in scale design, it uses observed information (here item responses) to discern unobserved information and to simplify this chaotic data into a parsimonious model (Hayton, Allen, & Scarpello, 2004). In an EFA model, every variable is correlated with every other variable and factor, but the strength of each association determines the underlying model structure (Yong & Pearce, 2013). These associations are expressed by the factor loading's regression coefficients, which measure the degree to which each/any factor influences a given item/variable (Fabrigar, Wegener, MacCallum, & Strahan, 1999). This technique is generally used when there is no underlying hypothesis to prove but there is a relational structure suspected (Finch & West, 1997). The original scale used sum scoring for the two constructs of 'social network' and 'social support'. However, it was theorised that the items in the scale described a more complex, nuanced environment existing on more than two dimensions. Due to the robust sample size and the variance of items, it was decided to undertake an EFA to divine the latent structure of this rich construct.

The backbone of measurement modelling is ensuring that the model selected best represents (or fits) the sample data. A poor-fitting model not only fails to describe the data but also increases the risk of Type 1 and 2 errors, producing potentially invalid conclusions. Various measures of model fit, fit indices, are analysis-dependant statistics used as guidelines when deciding on the best-fit model for the data. Different fit indices are used in these decisions as some are more resilient to data conditions such as sample size (Bollen, 1990; Fan, Thompson, & Wang, 1999; Hooper, Coughlin, & Mullen, 2008) but multiple indices are generally recommended (Fabrigar, Wegener, MacCallum, & Strahan, 1999).

The chi-square (χ^2), Root Mean Square Error of Approximation (RMSEA; Steiger, 1990), Tucker-Lewis Index (TLI; Tucker & Lewis, 1973), Comparative Fit Index (CFI; Bentler, 1990), and the Standardised Root Mean Square Residual (SRMR) were used to compare models generated in this analysis. The chi-square value in a fitted model should exceed 0.05 and is often considered the 'gold standard' in model fit testing (Barrett, 2007). However, the chi-square is vulnerable to sample size at both extremes, making it unreliable as the sole index for a model (Bentler & Bonett, 1980). While still a chi-square-based measure, the RMSEA is resilient to the effect sizes of a large sample and is parsimonious; it acknowledges that even the best-fit model is only ever an approximation of reality (Chen, Curran, Bollen, Kirby, & Paxton, 2008). The TLI is a non-normed fit index (NNFI) that is also resilient to sample size and should range between 0 and 1 (Hu & Bentler, 1999) with a larger value indicating a better fit; typically from .95 (Cangur & Ercan, 2015). Likewise, the CFI, developed by Bentler (1990), accommodates for population as well as comparing the covariance of the model against a null model (Hooper, Coughlan, & Mullen, 2008). As with the TLI, values are between 0 and 1 with .95 being a generally accepted threshold (Hu & Bentler, 1999). Lastly, the SRMR is the standardised delta between the observed and expected correlations, a measure of fit resilient to sample size and a variety of confounding conditions (Maydeu-Olivares, Shi, & Rosseel, 2018). As an absolute measure with 0 being a total fit between the observed and expected, a value less than 0.08 indicates a good fit (Hu & Bentler, 1999). The commonality in the fit indices chosen to evaluate this analysis is their accounting for sample size as this project deals exclusively with a large population sample.

Responses from the truncated social scale were prepared in IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp, 2018) as a .dat file and imported into Mplus 7 (Muthén & Muthén, 2012) for analysis. An exploratory factor analysis script was written and run on model designs from unidimensional to 5-factor with an oblique geomin rotation at 30 random starts and a maximum of 10,000 iterations.

3.3. Results

Respondent endorsements of each item in the truncated social scale (Table 3.1) show a fairly stable sub-sample of missing replies ranging from 20.01% to 22.17% of the total population (N=15,645). This population more than satisfied the 'rule of thumb' in sample size for factor analysis, with a sample >1000 classed as excellent for accurate results (Comrey & Lee, 1992).

Table 3.1. Populations and percentages for social scale item endorsement

	Response	Population	Valid Percentage
How many people are there that you can talk to about personal problems?	None	303	2.4
	1	1391	11.1
	2-4	7148	57.1
	>4	3672	29.3
	Missing	3131	
How many people talk to you about their personal problems or their private feelings?	None	240	1.9
	1	901	7.2
	2-4	6891	55.1
	>4	4471	35.8
	Missing	3142	
If you have to make an important decision, how many people are there with whom you can discuss it?	None	161	1.3
	1	1976	15.8
	2-4	6592	52.8
	>4	3757	30.1
	Missing	3159	
About how many friends do you have?	None	88	0.7
	1	113	0.9
	2-4	1368	10.9
	>4	10938	87.5
	Missing	3138	
During the last month, how many times did you get together with one or more friends?	None	651	5.2
	1	1038	8.3
	2-4	4439	35.5
	>4	6374	51
	Missing	3143	
During the last month, how many times did you get together with one or more of your relatives or your partner's relatives?	None	560	4.5
	1	992	7.9
	2-4	4391	35.1
	>4	6558	52.5
	Missing	3144	
I have no one to share my feelings with.	Exactly feel	125	1
	Often feel	441	3.6
	Sometimes feel	3350	27.1
	Never feel	8458	68.4
	Missing	3271	

Table 3.1 Populations and percentages for social scale item endorsement

There is always someone with whom I can share my happiness and excitement about my pregnancy.	Exactly feel	6975	56.9
	Often feel	3027	24.7
	Sometimes feel	1788	14.6
	Never feel	461	3.8
	Missing	3394	
How many of your family and friends would help you in times of trouble?	None	99	0.8
	1	323	2.6
	2-4	3798	30.4
	>4	8275	66.2
	Missing	3150	
If I was in financial difficulty I know my family would help if they could.	Exactly feel	9070	74
	Often feel	1606	13.1
	Sometimes feel	1054	8.6
	Never feel	535	4.4
	Missing	3380	
If I was in financial difficulty I know my friends would help if they could.	Exactly feel	4418	36.1
	Often feel	2387	19.5
	Sometimes feel	2841	23.2
	Never feel	2585	21.1
	Missing	3414	
There are other pregnant women with whom I can share my experiences.	Exactly feel	2875	23.6
	Often feel	2264	18.6
	Sometimes feel	3557	29.2
	Never feel	3479	28.6
	Missing	3470	
I believe in moments of difficulty my neighbours would help me.	Exactly feel	2858	23.3
	Often feel	2277	18.6
	Sometimes feel	3571	29.2
	Never feel	3537	28.9
	Missing	3402	
	Sample Total	15645	100

Table 3.2 shows the fit indices for this exploratory factor analysis, considering increasing dimensional models. Indices for a unidimensional through 5-factor model are shown. A 6-factor model with only 13 inventory items was too reductive and would not run. Here, a 5-factor model is the best fit for the sample data. The chi-square value for this model is markedly lower than the 4 preceding models and while it remains significant, it must be taken in conjunction with the other fit indices due to the large sample size of this analysis (N=12,549) and the chi-square's known vulnerability to sample size. The RMSEA is 0.037, less than 0.05, demonstrating the goodness-of-fit of this model. The TLI and CFI are both closest to 1 for the 5-factor compared to the other models. Lastly, the SRMR is approaching 0,

where an SRMR less than 0.08 indicates a good model fit (Hu & Bentler, 1999). Taken together, these fitness statistics support the 5-factor solution as the strongest measurement model with the given sample data.

Table 3.2. Fit indices for exploratory factor analysis

	χ^2	df	*p*	RMSEA	CFI	TLI	SRMR
1	6953	65	0.00***	0.092	0.775	0.730	0.063
2	2718	53	0.00***	0.063	0.913	0.872	0.036
3	2518	42	0.00***	0.069	0.919	0.850	0.030
4	921	32	0.00***	0.047	0.971	0.929	0.020
5	**412**	**23**	**0.00*** **	**0.037**	**0.987**	**0.957**	**0.012**

*** *indicates significance at ≤0.001; best fitting model in bold*

While useful in judging the most parsimonious model, fit indices are only one part of the exploratory factor analysis process. Parsimony is important in both mathematical and thematic results. Expanded below are the results of all exploratory models undertaken in this analysis, examined both for goodness-of-fit and conceptual utility to the thesis.

A unidimensional model returned factor loadings ranging from 0.315 to 0.744 (Table 3.3). A 2-factor model showed factor loadings ranging from -0.304 to 0.863 with a factor correlation of -0.481 (Table 3.4). A 3-factor model had factor loadings ranging from -0.266 to 0.860 and factor correlations ranging from -0.370 to -0.556 (Table 3.5). A 4-factor model provided factor loadings ranging from 0.285 to 0.903 and factor correlations ranging from -0.331 to 0.592 (Table 3.6). A 5-factor model yielded factor loadings ranging from 0.297 to 0.899 and factor correlations ranging from -0.284 to 0.592 (Table 3.7).

Table 3.3. Factor loadings for a unidimensional model

	Factor 1
# of people to confide in	0.744
# of people who confide	0.646
# of people to discuss decisions with	0.666
# of friends	0.443
meetings with friends in past month	0.506
meetings with relatives in past month	0.315
no one to share feelings with	0.497
someone to share excitement of pregnancy with	-0.455
# of helpers if in trouble	0.586
family would help with money	-0.443
friends would help with money	-0.504
other pregnant women to share experiences with	-0.382
neighbours would help if difficulties	-0.341

Table 3.4. Factor loadings and correlation for a 2-factor model

	Factor 1	Factor 2
# of people to confide in	**0.863**	-0.417
# of people who confide	**0.734**	-0.327
# of people to discuss decisions with	**0.672**	-0.426
# of friends	**0.382**	-0.353
meetings with friends in past month	**0.438**	-0.396
meetings with relatives in past month	0.239	**-0.304**
no one to share feelings with	0.386	**-0.506**
Someone to share excitement of pregnancy with	-0.274	**0.611**
# of helpers if in trouble	0.481	**-0.523**
family would help with money	-0.249	**0.626**
friends would help with money	-0.349	**0.573**
other pregnant women to share experiences with	-0.259	**0.436**
neighbours would help if difficulties	-0.217	**0.415**
Factor 1	1.000	
Factor 2	-0.481	1.000

Table 3.5. Factor loadings and correlations for a 3-factor model

	Factor 1	Factor 2	Factor 3
# of people to confide in	**0.860**	-0.325	0.390
# of people who confide	**0.733**	-0.242	0.327
# of people to discuss decisions with	**0.677**	-0.354	0.353
# of friends	0.382	-0.260	**0.410**
meetings with friends in past month	0.439	-0.279	**0.468**
meetings with relatives in past month	0.241	**-0.266**	0.261
no one to share feelings with	0.386	-0.410	**0.501**
Someone to share excitement of pregnancy with	-0.273	0.538	**-0.552**
# of helpers if in trouble	**0.489**	-0.486	0.366
family would help with money	-0.249	**0.811**	-0.309
friends would help with money	-0.357	**0.543**	-0.402
other pregnant women to share experiences with	-0.253	0.341	**-0.510**
neighbours would help if difficulties	-0.216	0.344	**-0.406**
Factor 1	1.000		
Factor 2	-0.370	1.000	
Factor 3	0.458	-0.556	1.000

Table 3.6. Factor loadings and correlations for a 4-factor model

	Factor 1	Factor 2	Factor 3	Factor 4
# of people to confide in	**0.903**	0.451	-0.373	-0.347
# of people who confide	**0.711**	0.446	-0.318	-0.235
# of people to discuss decisions with	**0.660**	0.393	-0.419	-0.311
# of friends	0.356	**0.474**	-0.290	-0.268
meetings with friends in past month	0.408	**0.778**	-0.335	-0.268
meetings with relatives in past month	0.221	**0.285**	-0.277	-0.228
no one to share feelings with	0.377	0.308	-0.366	**-0.547**
Someone to share excitement of pregnancy with	-0.253	-0.239	0.469	**0.762**
# of helpers if in trouble	0.460	0.392	**-0.568**	-0.329
family would help with money	-0.236	-0.192	**0.702**	0.486
friends would help with money	-0.328	-0.363	**0.609**	0.378
other pregnant women to share experiences with	-0.242	-0.300	0.314	**0.423**
neighbours would help if difficulties	-0.206	-0.227	**0.348**	0.346
Factor 1	1.000			
Factor 2	0.534	1.000		
Factor 3	-0.419	-0.426	1.000	
Factor 4	-0.347	-0.331	0.592	1.000

Table 3.7. Factor loading scores and correlations for a 5-factor model

	Trust	Contact	Sharing	Primary Support	Secondary Support
# of people to confide in	**0.899**	0.446	-0.329	-0.343	-0.260
# of people who confide	**0.714**	0.438	-0.199	-0.291	-0.242
# of people to discuss decisions with	**0.663**	0.389	-0.299	-0.397	-0.223
# of friends	0.362	**0.470**	-0.253	-0.258	-0.210
meetings with friends in past month	0.418	**0.782**	-0.240	-0.289	-0.265
meetings with relatives in past month	0.227	**0.297**	-0.253	-0.270	-0.050
no one to share feelings with	0.386	0.310	**-0.589**	-0.330	-0.219
someone to share excitement of pregnancy with	-0.267	-0.235	**0.709**	0.428	0.369
# of helpers if in trouble	0.467	0.393	-0.323	**-0.563**	-0.188
family would help with money	-0.245	-0.188	0.468	**0.703**	0.268
friends would help with money	-0.336	-0.349	0.314	**0.596**	0.383
Other pregnant women to share experiences with	-0.248	-0.279	0.369	0.252	**0.497**
neighbours would help if difficulties	-0.210	-0.195	0.264	0.307	**0.547**
Trust	1.000				
Contact	0.540	1.000			
Sharing	-0.343	-0.296	1.000		
Primary Support	-0.397	-0.361	0.494	1.000	
Secondary Support	-0.284	-0.296	0.340	0.330	1.000

Based on all analytical output (fit indices, factor loadings, and factor correlations) and conceptual fit, the 5-factor model was chosen as the most salient. The dimensions were given labels relating to the items which loaded onto them; Trust, Contact, Sharing, Primary Support, and Secondary Support. The factor correlation matrix for this model (Table 3.7) shows moderate positive correlations

between Trust and Contact and between Sharing and Primary Support. Trust and Contact are both negatively correlated with the other 3 factors, while Secondary Support is positively correlated with both Primary Support and Sharing.

With the analyses having yielded a salient, statistically well-fitting model for the sample data, the final undertaking was a graphic representation of the results. Figure 1 (below) shows the underlying structure of the prenatal maternal social environment. Scale item labels were reduced to an alphanumerical variable code to maintain figure simplicity; item loading remains as described in Table 3.9. The 13 items of the truncated social scale loaded onto 5 distinct, meaningful dimensions which in turn described this environment. Observed respondent data informed the unobserved structure of this previously abstract concept.

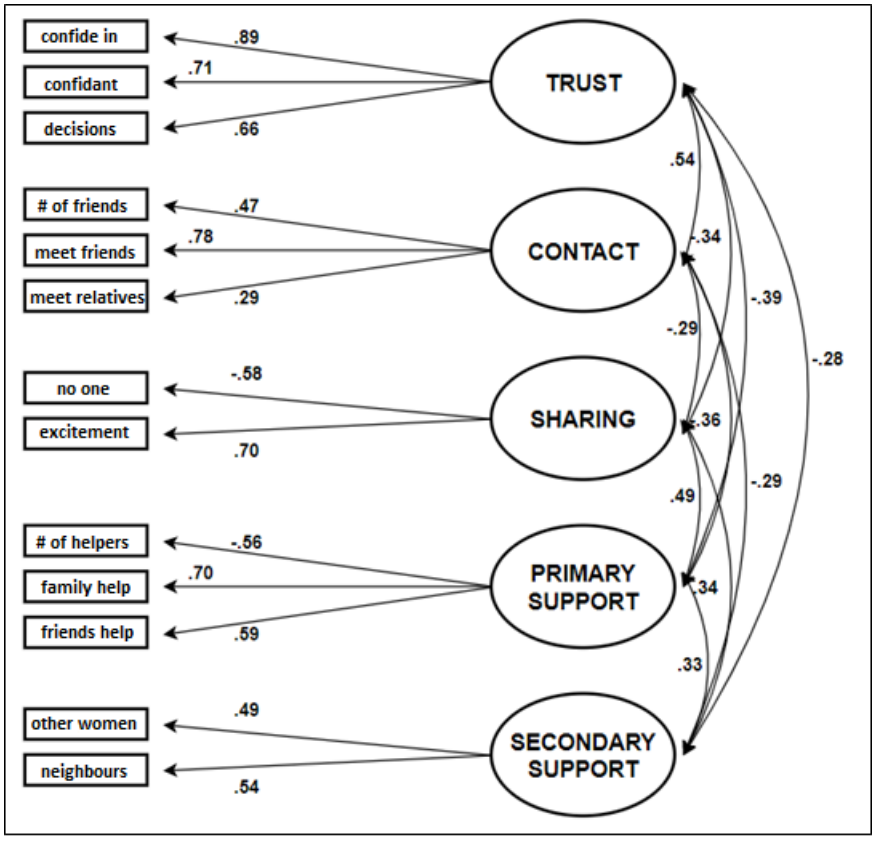

Figure 3.1. Factor model of the prenatal maternal social environment

3.4. Discussion

3.4.1. Model results and selection

This phase of analysis consisted of an exploratory factor analysis with 5 models of increasing complexity. The first analysis attempt assumed unidimensionality but the fit indices (Table 3.2) for this model show a poor fit for the data and the factor loadings (Table 3.3), did not support a unidimensional model. In examining the 2-factor model, the fit indices improved but the fit results were better for more complex models and though the factor loading scores also showed improvement, the fit was far from optimal. The 3-factor model was more complex, but the fit indices were poor and while the factor correlations improved, this model was rejected due to poor fit. The 4-factor model showed better fit than its simpler predecessors and the factor structure showed increased clarity in factor context, but the results for the 5-factor model showed a better fit.

Items ‘number of people to confide in’, ‘number of people who confide’, and ‘number of people to discuss decisions with’ loaded together onto a factor named *Trust*. Items ‘number of friends’ , ‘meetings with friends in the past month’, and ‘meetings with relatives in the past month’ loaded together onto a factor named *Contact*. Items ‘no one to share feelings with’ and ‘someone to share excitement of pregnancy with’ loaded onto a factor named *Sharing*. Items, ‘number of helpers if in trouble’, ‘family would help with money’, and ‘friends would help with money’ loaded onto a factor named *Primary Support*, while the remaining 2 items, ‘other pregnant women to share experiences with’ and ‘neighbours would help if difficulties’ loaded onto a factor named *Secondary Support*. ‘Primary’ and ‘secondary’ refer to degree of relationship intimacy; family and friends would be considered closer to the respondent than neighbours or non-friends/family pregnant women. The clarification of support into primary and secondary was the main contextual difference between the 4 and 5-factor models.

3.4.2. Dimensions of the prenatal maternal social environment

The 13 items from the truncated social scale aligned onto 5 factors, establishing dimensionality for the prenatal maternal social environment. These factors were named contextually based on which items loaded onto them, simplifying the scale (and the social environment) to 5 main themes. These factors were of contextual value and could also be used as a 'shorthand' in describing the prenatal maternal social environment and any participant's experience of the prenatal maternal social environment. The 5 factors could be further parsed into social dimensions (*Trust*, *Contact*, and *Sharing*) and support dimensions (*Primary Support* and *Secondary Support*), approximating the 'social network' and 'social support' sub-scales of the original metric. There were several items that 'switched sides' from their designation in the scale to this model, though this was most likely due the scale having been designed based on qualitative experience and not tested for quantitative purity. In EFA, 'factor loadings' represent the correlation between the observed and latent scores (Schmitt & Sass, 2011) and thus the closer to 1.0, the stronger the correlation. The factor loadings for the items in the final model showed moderate to strong loadings, with one notable exception described below.

Items '# of people to confide in' (.89), '# of people who confide' (.71), and '# of people to discuss decisions with' (.66) had a strong, positive loadings onto the factor *Trust*. These items were categorial representations of continuous variables and their alignment onto the factor *Trust* was not dependant on any perception of trust by the respondents. Rather, because the 3 items are each representative of aspects of a trusting relationship and the quantity of those trusting relationships, the factor they loaded onto became endemic of trust in the prenatal maternal social environment.

Trust can be used to describe a relationship's depth of intimacy (Lewicki & Bunker, 1995). It is well established that women are more likely to rely upon friends in difficult times and prioritise emotional self-disclosure in friendships (Roy, Benenson, & Lilly, 2000). This intimacy is a mutable construct, as trust can be gained or lost depending on the circumstances of intimate relationships. Existing on both emotional and rational levels, trust is a positive contributor to emotional and mental well-being (DeNeve & Cooper, 1998). DeNeve (1999) suggests that trust is a

facet of social competence promoting happy relationships while Lahno (2001) describes it as a mechanism for coping with interpersonal risk. As members of a social species, human beings rely on each other and being able to trust another with potential survival is vital (Bateson, 1988). Emotionally, trust can be considered alongside the Hierarchy of Needs (Maslow, 1943) as a safety need akin to emotional security, to the point that trust defines the earliest stage in Erikson's developmental model (Erikson, 1959). This is an integral part of not only human growth and development, but also of mental health and well-being throughout the lifespan. A participant having multiple people she could trust may have reduced the stress of pregnancy (Orr, 2004; Drentea & Moren-Cross, 2005) and could have potentially signalled to the foetus' that it would be born into a caring, nurturing environment.

Items '# of friends' (.47), 'meetings with friends in the past month' (.78), and 'meetings with relatives in the past month' (.29) loaded onto the factor *Contact*. The item 'meetings with relatives' had a relatively low loading score but this was the strongest loading relationship among the 5 factors. It is possible that the scale primarily described friend/acquaintance relationships with familial relationships and interactions as an outlier. This item was retained pre-analysis as it captured instances of face-to-face interaction and socialisation cannot be conceptualised as just friend/acquaintance relationships.

As a social species, humans are geared towards personal contact. *Contact* here described face-to-face interaction and quantity of that interaction, recognising it as an independent dimension. It is well accepted that contact is vital to human socialisation, to the extent that humans in physical isolation suffer cognitive decline (Cacioppo & Hawkley, 2009; Lara et al., 2019) and symptoms of psychopathology including depression (Alpass & Neville, 2003; Taylor, Taylor, Nguyen, & Chatters, 2018), anxiety, (Chou, Liang, & Sareen, 2011), and psychosis (Broome et al., 2005; Reininghaus et al., 2008). Whereas *Trust* and *Sharing* were more emotional and the support factors more material, *Contact* was the most evolutionarily based of the dimensions in this model. Human beings have a biological need for contact (Belsky, 1981; Carpendale & Lewis, 2004) though individual desire for contact varies in any given population and can be situationally or culturally dependant. In addition, *Contact* was the only objective factor in the model as the other 4 factors depended on

the respondent's subjective perceptions. When cortisol crosses the placental barrier, it does so during both subjective and objective prenatal stressors (Laplante, Brunet, Schmitz, Ciampi, & King, 2008). While *Trust* and *Sharing* spoke to the emotional connections of the social environment, *Contact* was physical. It was hypothesised that this factor would be important not only in defining how these dimensions typified groups within this sample, but also regarding the behaviour of the eventual offspring.

Items 'no one to share feelings with' (-.58) and 'someone to share the excitement of pregnancy with' (.70) loaded onto the factor *Sharing*. This factor, existing independently of *Trust*, isolated an aspect of socialisation present in many different types of relationships. *Sharing* was defined in this model by the underlying intimacy of sharing rather than the presence of the word 'sharing' in the item. For example, the item 'other pregnant woman to share experiences with' loaded onto a different factor (*Secondary Support*) as it described the less intimate sharing of 'experiences' over sharing the more intimate 'feelings'. It was also implied that participants had in mind a specific individual for the item 'someone to share the excitement of pregnancy with', again implying intimacy.

The independence of this factor from *Trust* suggests a separate type of relationship intimacy. As a concept outside of this model, sharing is not beholden to any specific relationship type, as a person with which to share feelings and excitement with could be a partner, friend, or relative. Whereas trust may imply a more intimate facet of a relationship, sharing implies a commonality or an empathic connection. The want to share with another can imply a certain degree of trust but the parameters of sharing often depend on what information is being shared and with whom. Sharing is also a mutual activity, requiring a 'giver' and 'taker', though the items loading onto the *Sharing* factor had a more egalitarian connotation. In the context of this model, the action of sharing was externalising internal thoughts and feelings and feeling comfortable doing so.

Items '# of helpers if in trouble' (-.56), 'family would help with money' (.73), and 'friends would help with money' (.59) loaded onto the factor *Primary Support*. This factor described the expectation of support, either monetary or

unspecified ‘help’. The ‘primary’ designation described both the calibre of the support and the intimacy of relationship between the respondent and the supporters. That the ‘helper’ item loaded onto *Primary Support* indicated that the respondents felt that help when ‘in trouble’ (with trouble being subjective to the individual) was comparable to monetary support.

Human survival has always depended on the collective nature of families, communities, and societies (Bowles & Gintis, 2002; Boyd, 2006; Boyd & Richerson, 2009). An expectation of helpers in an emergency or the monetary support of family/friends is an expectation of security and ultimately survival. As per Maslow (1943), the physiological needs (air, water, food, shelter, clothing, etc.) are the most basic and vital. Poverty threatens an individual’s access these necessities (Harper, Harper, & Stills, 2003) and the potential for dire straits following a personal emergency is a constant threat of contemporary existence. Personal security and resources are among the safety needs in the next step of the hierarchy (Maslow, 1943) and they are also at risk when money is tight. Thus, inadequate resources and/or no expectation of resource support is considered a significant prenatal stressor (Lefmann & Combs-Orme, 2014). Resource deficit could also directly threaten the foetus; maternal malnutrition leads to a ‘crisis measure’ whereby foetal development prioritises vital systems (brain, lungs, etc.) by sacrificing overall growth, gambling on adequate resources after birth (Gluckman, Hanson, & Low, 2019).

Items ‘other pregnant women to share experiences with’ (.49) and ‘neighbours would help if in difficulty’ (.54) loaded onto the factor *Secondary Support*. Here ‘secondary’ indicated auxiliary support from non-proximal people in the respondent’s life. The ‘other pregnant women’ and ‘neighbours’ are categorically separate from friends and family, with relational proximity working as a hierarchy, i.e., friends and family who are pregnant and/or neighbours would be assumed to belong to the former category over the latter. This act of sharing experiences required less personal commitment than monetary support and the phrase ‘in difficulty’ was semantically weaker than ‘in trouble’, regarding the ‘# of helpers if in trouble’ item loading onto *Primary Support*.

Though varying by culture, society, or even region, neighbour relationships are generally not as intimate as family/friend relationships (McGahan, 1972; Jamieson, Morgan, Crow, & Allan, 2006) and there is a lesser expectation of support. This was also true of relationships with 'other pregnant women' who did not fall into the family or friend dynamic. For example, a local expectant mothers' social group or an acquaintance relationship based on the pregnancy would be lower on the intimacy hierarchy than long-time friend or family member who was also pregnant. When examined in context to the other 4 dimensions, *Secondary Support* may seem the least important considering the main hypothesis. However, small kindnesses and the ability to rely on support when intimate-relationship individuals are not available (or do not exist) has value to individuals in need (Warburton & McLaughlin, 2005; Cleary & Horsfall, 2016). While specific profiles within the population had not yet been identified, it was hypothesised that a sub-population may have existed for whom *Secondary Support* constituted their main support.

The relationships between factors in this model were described by factor correlations (Table 3.7), which ranged from low to moderate. *Trust* and *Contact* had the highest correlation in the model (0.546). *Sharing* and *Primary Support* were moderately correlated (0.494), as were *Trust* and *Primary Support* (-0.397), *Contact* and *Primary Support* (-0.361), *Trust* and *Sharing* (-.0343), *Sharing* and *Secondary Support* (0.340), and *Primary Support* and *Secondary Support* (0.330). *Contact* and *Sharing* (-.0296), *Contact* and *Secondary Support* (-0.296), and *Trust* and *Secondary Support* (-0.284) showed lower factor correlations.

3.4.3. Model discussion

This model was a representation of the prenatal maternal social environment as described by the lived experiences of ALSPAC's maternal cohort. It defined the dimensional structure underlying the relationships these mothers-to-be enjoyed (or did not enjoy) along 5 contextually relevant factors which were tested and found to be the best fit for the data used. In addition to simplifying the item-level responses of a large population (N=12,549 after missing cases dropped), the dimensional model could then be used as a foundation for the sequential analyses in this project. The

salience in this analysis was using statistical techniques to summarise data and give form to the somewhat nebulous concept of the social environment. Attitudinal data may seem imprecise; what is the practical difference between a score of 11 and 12 on a depression inventory? What does 1 point of 'depression' look like or feel like? The metrics used to collect attitudinal data for quantitative analysis allow for those vague feelings to be codified and standardised. This was the true value of the primus analysis here.

The attitudinal data used in this analysis was taken from a scale used in qualitative studies and divided into social network and social support subscales, contextual halves mirrored in the dimensions identified here. Both parts were important in defining the prenatal maternal social environment, as the network aspect described quantity and frequency of objective contact alongside the subjective experiences of that social contact, while the support aspect described depth of subjective expectation of monetary and emotional support together with the objective reality of sufficient/insufficient support as a stressor. Though this scale was not specifically designed to have a purely quantitative use, it was nevertheless valuable in describing a more complex view of the prenatal maternal social environment. This allowed for the contextualisation of socialisation to be more a nuanced environment and less a binary state of 'social' or 'isolated' or a simple socialisation score.

Each of the 5 dimensions was a descriptor of that environment and different rates of endorsement along those dimensions conveyed the personal experiences of respondents. The ability to then describe members of the population by those dimensions meant the ability to identify specific sub-groups in the sample. In this way, it was possible in the next analysis to find patterns of socialisation that typified the prenatal maternal social environment in this cohort. As an example, a participant with a higher endorsement of *Trust* and *Sharing* had a very different experience of socialisation from one with lower endorsement. It was predicted there would be significant variance in this population in terms of socialisation and having discreet measures to describe that variance led to the obvious research question; what in/about the lives of these women might have contributed to their social environment and were these variables able to reliably predict respondents' picture of

socialisation? There was a wealth of information in who could be described by what rate of endorsement on which factor and what that would ultimately mean for their offspring.

3.4.4. Limitations

These results must be considered with respect to the limitations of this study. The social scale used by ALSPAC was neither created nor tested for the specific purpose of this thesis. Its design was based on a qualitative interview schedule rather than for quantitative analysis. Items were dropped in cases of contextual covariance (borrowing £100 vs. general monetary support) and to preserve model homogeneity (a binary item in a predominantly Likert scale). Cases with missing data were dropped from the analysis and while the attrition was only 20%, results here only represented the analytical sample (N=12,549) rather than the population sample (N=15,645). Data used in this analysis were limited by resource availability and confined to the variables ALSPAC collected. Assuming unlimited resources, this analysis would have included additional attitudinal variables describing the mothers' perceptions and mental state during and directly preceding the first trimester. Assuming that data collection had been designed with this thesis in mind, multiple measures describing socialisation, loneliness, and lifetime social preferences would have been utilised. Data collection took place before the advent and popularity of social media, meaning contemporary replication attempts will need to either control for its effects or incorporate it into the study design. Finally, these results are specific to the ALSPAC maternal cohort, which may be generalised to the greater UK population (Golding et al., 2001), but no farther.

3.4.5. Impact and implications

The model resultant of this analysis has impact beyond this project. Understanding multimodal constructs like social environments from an empirical, data-driven viewpoint can both simplify and standardise research. When statistically robust methodologies are employed, it benefits the original analyses, replication

studies, and meta-analyses/systematic reviews. Environmental modelling in the social sciences could also be used in psychometric design and testing. For example, modelling an adult social environment based on demographics and unrelated items could underpin the creation of a factor-tested attitudinal scale measuring perceptions and effects of that environment. This process could have applications across the field; modelling interactions in an in-patient mental health facility to then design a scale to determine what effect the in-patient environment had on personal recovery, etc.

Understanding the prenatal maternal social environment and its underlying dimensions will also provide the ability to consciously affect that environment. Social isolation is well understood to be harmful to the individual and more research is demonstrating that the stressor of isolation is harmful to the growing foetus, constituting a mandate for action. Social isolation has been recognised as a major causal factor in loneliness, which carries significant risk to physical and mental health (Mushtaq, Shoib, Shah, & Mushtaq, 2014; Beutel et al., 2017). A robust empirical model for such an environment is a platform upon which to build programs and policy. Clinical schedule questions based on the factors of the prenatal maternal social environment could be used during GP visits to flag women in social isolation, regardless of distress level. The GP could then refer the patient to local community groups, pregnant mother social groups, or even to a mental health professional in extreme cases of isolation (or if there are other underlying issues). Such initiatives would focus on the woman and the unborn child, stressing the importance of socialisation to her health/well-being and crucially, that of her child. Programs to address the immediate problem of isolation would greatly assist the mother and child but higher-level policy could address the systemic issues that contribute to social isolation in a population.

Discounting the project thesis, modelling the prenatal maternal social environment was an example of a research contribution with a potential practical benefit. Understanding what constitutes normative and deficit environments and their potential outcomes naturally leads to preventative methods for these outcomes. As early as 1843 (Maloni, Cheng, Liebl, & Jeanmarie, 1996), the medical field had begun to recognise that the health needs of pregnant women were more complex

than just ‘human being +1’. As with so much in the history of medicine, practice leads to protocol. For example, with the discovery of the importance to folic acid in pregnancy (Wills, 1931), specifically to foetus’ spinal cord development (Hibbard & Smithells, 1965), health guidelines changed to reflect the need for folic acid from pre-conception through at least 12 weeks gestation (World Health Organisation, 2007). With publication, the model of the prenatal maternal social environment in the ALSPAC cohort described here can now be subject to replication studies, both in-cohort and in similar large population samples.

3.4.6. Conclusions

This chapter utilised a simplified 13-item scale on prenatal socialisation in an exploratory factor analysis, identifying a 5-factor structure underlying the prenatal maternal social environment. Contextually, the analysis in this chapter used large population data to conceptualise an ephemeral concept as an empirical model, a foundation on which further analytical phases could be built. As it was hypothesised that aspects of the prenatal maternal social environment would have an effect on the foetal genome, modelling this environment was the first step in testing this hypothesis. The next step was to statistically examine the prenatal maternal social environment to determine if specific patterns or sub-population profiles existed within the population cohort, based on the dimensional structure established in this chapter. Understanding variance in this sample and codifying ‘high socialisation’ and ‘isolation’ in the population would allow for further testing of offspring of these bespoke profiles within the maternal cohort.

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Chapter 4

Specific profiles within the maternal population

4.1. Study Introduction

In the previous chapter, data from a scale describing socialisation was used to establish the underlying structure and dimensionality of the prenatal maternal social environment in the study population. While that model was valuable when discussing that environment, it said very little about the women who existed within it. The prenatal maternal social environment was defined by *Trust*, *Sharing*, *Contact*, *Primary Support*, and *Secondary Support* and so each respondent could then be defined in the same way, by their scores along these dimensions. The ultimate goal of this project was to compare the offspring of mothers in both high and low prenatal maternal social environments to determine functioning in 'mismatched' social environments, with the hypothesis being that epigenetic priming would contribute to that functioning. Having created a structure for the prenatal maternal social environment, the next step was to use that structure in measuring socialisation while determining what sub-samples within the maternal population were high or low. Where the previous chapter built the analytical house, work in this chapter decided who lived in which room and why.

The undertaking was in selecting appropriate analytical techniques for these aims to find models that best fit the data by grouping respondents together by their endorsement of proxies, the environmental dimensions. These distinct groups within the larger population would be typified by level of socialisation, identifying high and low. Profiling this variation also meant describing it in terms of the respondents; who were these women and why did they belong in these groups? Utilising the wealth of data collected by ALSPAC during the prenatal period, it was possible to stratify these groups based on the commonalities of their members and identify what about each woman's life could 'predict' what group she would be assigned to. Variation in socialisation and meaningful description of the resultant groups allowed for the maternal cohort to be described in terms which could then be carried through to the offspring cohort. A child of a high or low socialisation mother could then thus identified as the thesis hypothesis was tested during their adolescence.

It was decided that a latent profile analysis afforded the ability to organise the maternal population by socialisation profile and that a logistic regression of chosen covariates to isolate profile predictors could further describe those profiles.

4.1.1. Latent Profiles in a Population

This phase of analysis undertook a latent profile analysis (LPA), a type of latent modelling developed for attitudinal survey analysis (Lazarsfeld & Henry, 1968 as cited in Magidson & Vermunt, 2004). It identifies sub-groups within a population by assigning respondents membership in discreet groups based on the analytical parameters set by the researcher (Lanza, Collins, Lemmon, & Schafer, 2007). As the parameters used here were both categorical and continuous variables, group membership was mutually exclusive rather than probabilistic. In addition, latent groups are a contextually meaningful summary of endorsement data, especially in a large population. This technique has been brilliantly applied in mental health research to identify symptomatically divergent groups and better assess and address their needs. Butter, Shevlin, and Murphy (2018) examined the continuum of negative self-evaluation to differentiate between poor mood outcomes, self-harm, and suicidality (see also Klonsky & Olino, 2008 for distinct sub-groups among self-injurers). Autism Spectrum Disorder (ASD) often presents as a constellation of traits/symptoms with expressions that change over time and latent analysis has been used to track child trajectories (Landa, Gross, Stuart, & Bauman, 2012; Spikol, McAteer, & Murphy, 2019). Lanza and Rhodes (2011) even proposed latent class analysis as an alternative tool in analysing individual responses to specific treatment methods.

Like EFA, latent analysis can also describe abstract concepts that underlie categorical data. For example, data from a personality inventory could be used in an LCA to identify groups exhibiting specific traits, attitudes, or beliefs, all defined as different styles of ‘temperament’ (Loken, 2004; Rettew, Althoff, Dumenci, Ayer, & Hudziak, 2008). In the undertaking of this project, it was hypothesised that the prenatal maternal social environment was comprised of distinct dimensions but also that respondents could be characterised by their variation across these dimensions.

‘Socialisation’ is a nebulous abstract concept but here was summarised as an expectant mother’s alignment along the dimensions *Trust*, *Sharing*, *Contact*, *Primary Support*, and *Secondary Support*. While definitions like this extend only to the work at hand, having concrete meanings for the abstract allow for a wealth of social science research to be done, as well as aiding in replication studies.

Profile specificity was particularly important to the thesis hypothesis, which centred on environmental interaction with the foetal genome to produce specific outcomes in specific circumstances. To posit that prenatal maternal social isolation caused an epigenetic effect that ‘insulated’ offspring from the negative effects of isolation meant defining to whom in the sample the thesis applied. Longitudinal studies with smaller sample sizes theoretically have the ability for in-depth individual tracking of participants but this strategy was not a viable option for a large population (N=15,645). Identifying classes within the sample was the most appropriate method for determining high and low socialisation groups and allowing for longitudinal tracking of offspring outcomes. In addition, LPA was able to concisely summarise a large population sample in a way that was contextually salient. Respondents were assigned profile membership based on their endorsement of items from the social network/social support scale given at 12 weeks gestation which aligned to the 5 dimensions of the prenatal maternal social environment.

4.1.2. Regression and Covariate Predictors

LPA was used here to derive salient classes from the population and while it explained how the groups differed, it did little to explain why they differed. Once the profiles were identified as distinct, they could be explored to the fullest extent of the data available. Specifically, the goal was to uncover anything that might ‘predict’ that an individual would be a member of one group and not another. Using covariates in a mixed model or alongside of a latent model allows for the understanding of individual, sub-group, and population in one simple analysis. A logistic regression of chosen covariates on the groups yields an odds ratio likelihood relationship between that covariate and group membership. This analytical strategy has been used successfully across the field from defining predictor motivations of

online multi-user games addiction (Hussain, Williams, & Griffiths, 2015), to socio-demographic variables predicting health profiles in elderly individuals (Ng, Luo, & Heng, 2014), to traumatic risk factors and clinical variable predictors of psychosis symptomology (Shevlin, Murphy, Dorahy, & Adamson, 2007). Such predictors can also be important in informing clinical practice (Kline, 1991; Adams et al., 2016) and potentially in forming health policy.

Predictor covariates enrich understanding about groups in the population as these variables relate to the research question. The covariates chosen for analysis here were used due to their relationships with socialisation, both positive and negative. This allowed for both exploring the characteristics of the high and low socialisation groups but also provided potential confounding variables for later consideration. When putting forward the idea that the prenatal maternal social environment has an effect on offspring socialisation, other influences must be identified and controlled for. These covariates affected the mother's prenatal socialisation but could have also influenced the child during the postnatal period. Incorporating them into the model at this stage of the project allowed for their effects to be identified and later controlled for, if necessary. Regarding socialisation, there was potentially an infinite number of factors to consider, both internal and external (environmental). It was decided that a bank of covariates be selected from the available data to explore and these demographic, attitudinal, and adverse covariates were selected based on the supporting literature.

The mother's age at 8 weeks gestation, the presence of a partner, and socio-economic status (SES) were chosen as demographic covariates in this phase of the analysis. Human social behaviour is dependent on a multitude of factors, but it is well established that social relationships change from early childhood through adulthood, changing in quality and quantity (Pinquart & Sörensen, 2000; Carmichael, Reis, & Duberstein, 2015). Age was included to catch any potential age effect present in this population. While the presence of a partner was excluded from the socialisation model, it was included as a covariate here as membership in an intimate relationship can affect friendships and depth of social relationships in adult women (Tschann, 1988; Voss, Carbery & Buhrmester, 1998; Markiewicz, & Doyle, 1999). SES was utilised due to its multifactorial impact on the individual: higher

SES is associated with better physical health and wellbeing (Taylor & Seeman, 1999; Goldman & Smith, 2002) and lower SES with poor health and mental health outcomes (Baum, Garofalo, & Yali, 1999; Blakey, Hales, & Woodward, 2004; Nandi, Glymour, & Subramanian, 2014). Specifically, homogeneity of SES among friends (Brown, 1981; Chan & Goldthorpe, 2004) and the propensity of higher SES individuals for increased friend and friendship diversity (Smith, 2018). In addition, SES affects social mobility with individuals on the lower end of the scale facing restricted social mobility (Power, Matthews, & Manor, 1996; Heinonen et al., 2006).

Two attitudinal covariates were included: neighbourhood quality and interpersonal sensitivity. While neighbourhood quality could be seen as linked to SES, the definition of 'quality' is based entirely on individual perception and not on any objective measure, such as property tax or mean income. This variable was chosen as a covariate as negative perceptions of neighbourhood quality can negatively affect individual attitudes across multiple domains (Connerly & Marans, 1985; Greenberg, 1999; Parkes, Kearns, & Atkinson, 2002) but positive perceptions have a positive impact on mobility (Boehm & Ihlanfeld, 1986). A neighbourhood that feels unsafe or where residents do not feel secure struggles to foster the same adult social networks found in higher quality areas (Carpiano, 2007), meaning fewer local opportunities for socialisation. When considered in conjunction with a potentially lower SES preventing an individual from living in a higher quality neighbourhood, living where it is unsafe may preclude most socialisation entirely.

Interpersonal sensitivity (IS) has a moderating relationship with rejection sensitivity and interpersonal social competence (Butler, Doherty, & Potter, 2007) in addition to correlating with the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1964). This correlation is important when recalling one of the driving theories of this thesis; extraversion is a factor in socialisation-seeking behaviour in individuals and varies in the population as a function of individual differences. IS also correlates with neuroticism (Gillespie, Johnstone, Boyce, Heath, & Martin, 2001; Wilhelm, Boyce, & Brownhill, 2004; Bishop, Herrick, Stowe, Golding, & the ALSPAC Study Team, 2008) but has also been shown to be a strong predictor of depression (including post-partum depression) (Boyce, Hickie, & Parker, 1991; Boyce et al., 1992; Luty, Joyce, Mulder, Sullivan, & McKenzie, 2002),

anxiety/social anxiety (Harb, Heimberg, Fresco, Schneier, & Liebowitz, 2002; Vidyanidhi & Sudhir, 2009), and parental bonding (Boyce, Hickie, & Parker, 1991; Todd, Boyce, Heath, & Martin, 1994).

IS was an important covariate during this analysis but also as a potential confounding variable in later stages of the project. Maternal IS was found to be positively associated with social issues in offspring, mediated by child emotional dysregulation (Suveg, Jacob, & Payne, 2010). Prenatal maternal IS also predicted infant-mother relationship quality at 1 year in a sub-sample of the ALSPAC population (Raine, Cockshaw, Boyce, & Thorpe, 2016), though the authors note that higher scores are predictive of depressive symptoms. There is evidence of a genetic component to the variation in IS (Gillespie, Johnstone, Boyce, Heath, & Martin, 2001) and that the brain derived neurotrohic factor (BDNF) *Val66Met* influences IS in children/adolescents (Chen, Li, & McGue, 2012; Suzuki et al., 2012; Ibarra et al., 2016) while Chen et al. (2015) found maternal IS and anxiety moderated *Val66Met* in neonatal brains. IS could inform some of the variance in socialisation differences across the child cohort and was a variable to potentially control for in the aggregate model.

Five adverse covariates were selected from the extant data: life events, experience of discrimination, depression, childhood home instability, and childhood abuse (both stranger and non-stranger). These covariates were concrete in nature, meaning they were either present or not. Childhood home instability was derived from an attitudinal scale (details below) but included on a contextual basis as an adverse covariate. It is important to stress that the experience of these adverse covariates was expected to have a negative effect on overall socialisation while their absence was hypothesised to have a positive effect. In the scope of this analysis, life events, childhood home instability, and childhood abuse were considered as trauma. Trauma's effects on the individual can be catastrophic and far-reaching, with a significant impact on social functioning and adult relationships (Busby, Walker, & Holman, 2011; Rholes, Paetzold, & Kohn, 2016), mediated by trauma's contribution to mental distress/psychopathology (Bolton, Hill, O'Ryan, Udwin, Boyle, & Yule, 2004). In addition, home instability can affect attachment style (Bederian-Gardner et al., 2018), and is associated with behavioural issues (Ackerman, Kogos,

Youngstrom, Schoff, & Izard, 1999; Fomby & Cherlin, 2007) and an increased risk of psychopathology (Adam & Chase-Lansdale, 2002). Beyond the effects of the trauma of childhood abuse, similar trust issues (Cross, Koh, Rolock, & Eblen-Manning, 2013) and intimate relationship issues are possible (Ackerman, Kogos, Youngstrom, Schoff, & Izard, 1999; Tsai & Rosenheck, 2012).

The experience of discrimination was left open concerning the perceived reason for the event (see below) and was not confined to race/ethnicity. It was proposed that the contextual trauma of discrimination would have an adverse effect on socialisation for the women who experienced it. Discrimination has shown a direct relationship with depression (Noh, Beiser, Kaspar, Hou, & Rummens, 1999; Finch, Kolody, & Vega, 2000, moderated by nativity status; Belle & Doucet, 2003; Schultz et. al, 2006). Experiences of discrimination are reported to factor into depression as the individual pulls away from others to avoid additional events or out of the belief that others "*wouldn't understand*" (Negi, 2013, pp. 171). This can create a vicious circle of discrimination leading to social isolation, which in turn feeds exclusion and further events (Oxman-Martinez et al., 2012). It is ironic that discrimination might drive an individual away from socialising, as Pascoe and Richman (2009) found, in a meta-analysis of 15 studies, social support (both instrumental and emotional support) partially moderated negative health outcomes due to perceived discrimination.

Depression is well known for negatively affecting an individual's life and ability to function across multiple indices. Major indicators of clinical depression include persistent sadness/low mood, anhedonia (lack of pleasure or interest), fatigue, poor self-confidence, and feelings of guilt or self-blame (World Health Organisation, 1992). These manifestations of distress can limit socialisation by removing the desire/will to be social (Wei, Russell, & Zakalik, 2005; Kelly et al., 2011), or causing the individual to withdrawal from socialisation entirely (Schreiter, Pijnenborg, & aan het Rot, 2013), which in turn can worsen depressive symptomology (Teo, Choi, & Valenstein, 2013). This is not to suggest that an individual with depression will be unable or unwilling to socialise, only that it constitutes a significant barrier to the process. As it is well established that social support can moderate the distress of depression and similar psychopathologies

(Schumm, Briggs-Phillips, & Hobfoll, 2006; Vranceanu, Hobfoll, & Johnson, 2007; Santini, Koyanagi, Tyrovolas, & Mason, 2015), this creates a particularly tragic vicious circle. It was hypothesised here that the experience of depression would be an important predictor covariate of low socialisation in this cohort.

4.1.3. Study Aims

This thesis has posited that the stressors implicit to social isolation during pregnancy trigger an epigenetic modification meant to prime the offspring of isolated mothers for a persistent environment of isolation. The social environment of highly socialised mothers would not require such an adaptation in the offspring genome. Thus, when the offspring with phenotypical priming encountered a deficit social environment, they would be prepared, while the other offspring sub-sample would not, and would incur increased adaptive psychopathology. It was also considered that the phenotypically primed offspring could potentially be stressed/distressed when in a highly socialised environment. To make the distinction between offspring it was necessary to determine what constituted high or low socialisation in this population and to differentiate between those groups. It was also important to isolate what personal or environmental variables predicted the prenatal maternal social environment for respondents, as those factors could have a legacy effect on offspring socialisation and psychopathology beyond any epigenetic effect.

The ultimate aim of this phase of the analysis was to discriminate between high and low socialisation sub-samples within the main population. This was accomplished by using the 5 dimensions of the prenatal maternal social environment in a latent profile analysis to model levels of socialisation and categorise the cohort by that model. It was hypothesised that these profiles would portray high, low, and ‘mean’ levels of socialisation and that these groups would be meaningful. Following on from this, ancillary covariate data was used in a logistic regression to identify predictors of profile membership and to what extent they influenced that membership. It was further hypothesised that these covariates would describe the groups in a similarly meaningful way.

4.2. Methods

4.2.1. Sample

The sample pool for this phase of the analysis consisted of the ALSPAC maternal cohort (N=15,645) and cases with missing data were dropped, resulting in a sample size of (N=12,549). Mean age for this population was 27.77 years (SD=4.91 years) with a range of 15-45. Most respondents had lived in the Avon catchment area for at least a year: 53.4% had lived in/near Avon all their lives, 16.9% over 10 years, 11.2% between 5 and 9 years, 13.6% between 1 and 4 years, and 5% for under a year (Herrick, Golding, and the ALSPAC Study Team, 2008). The population was further described as 79.1% homeowners, 79.4% married, and 97.8% were white/Caucasian (Fraser et al., 2013).

4.2.2. Measures

Covariate data was sourced from the mother-based self-complete prenatal questionnaires ‘Your Environment’ (8 weeks gestation), ‘About Yourself’ (12 weeks gestation), ‘Having A Baby’ (18 weeks gestation), and ‘Your Pregnancy’ (32 weeks gestation). These covariates included socioeconomic status, neighbourhood quality, interpersonal sensitivity, adverse life events, experience of discrimination, experience of depression, home stability, abuse, presence of a partner, and age. Covariate descriptions and methodology can be found in Chapter 2 (Section 2.5.2).

4.2.3. Analytic Strategy

4.2.3.1 Step 1: define distinct profiles

Latent profile analysis (LPA) was performed with Mplus 7 (Muthén & Muthén, 2012) to create a measurement model of the population. This technique uses observed data as means to explore the population to detect previously unobserved

(latent) groups, or profiles, and any given respondent's 'membership' in these profiles based on that data. LPA was developed for use in the social sciences as a method of analysis for attitudinal surveys but has seen ever-broadening applications over the past several decades (see Nylund, Asparouhov, & Muthén, 2007). A series of LPAs was run to determine the best model for this population, testing 7 models in a 2-class through 8-class solution, using respondent factor scores along the dimensions of *Trust*, *Sharing*, *Contact*, *Primary Support*, and *Secondary Support* describing the prenatal maternal social environment at 12 weeks gestation.

A range of common fit indices were used to compare the models. To determine the best fit, the Akaike information criterion (AIC, Akaike, 1987), the Bayesian information criterion (BIC, Schwarz, 1978), and the sample size-adjusted Bayesian information criterion (SSABIC, Sclove, 1987) were used. The AIC functions as a quality determinant for models against each other and while it cannot provide the absolute quality of any given model, it can inform on the best among models, providing a log likelihood. Related to the AIC, the BIC relies on Bayesian inference but is susceptible to sample size where the sample exceeds the number of parameters, thus the SSABIC can be used in tandem to correct for larger populations. The lower these indicators, the better the model fit. This analysis utilised the Lo-Mendel-Rubin likelihood ratio test (LMR-LRT, Lo, Mendel, & Rubin, 2001) as another comparison index. This test commonly compares a model with k number of profiles with a model featuring $k - 1$ profiles. In an LPA, a non-significant result in the LMR-LRT p-value demonstrates the model with $k - 1$ profiles is the better fit. The entropy criterion (Celeux & Soromenho, 1996) was the final statistic used to assess model fit. Entropy can be described simply as the amount of uncertainty or 'surprise' in any variable's outcomes as a function of its probability (Shannon, 1948). In this analysis, it used posterior probabilities to assess the accuracy of an individual's assignment to a profile. Values for entropy range from 0 to 1, meaning a higher entropy value would convey a more accurate classification of the individual into a specific profile.

Cross-validation with multiple fit indices was beneficial to the analysis as it ensured that no one (potentially fallible) statistic was responsible for determining the best fitting model. Nylund, Asparouhov, and Muthén (2007) discuss the points of

which criterion is the most useful in determining the optimal latent profile model, with no clear consensus between BIC and LMR-LRT. As the LMR-LRT is vulnerable to over-classification when sample size is >1000 (Tofighi & Enders, 2008), and given the large population in this analysis, the BIC was recognised as the more accurate determinant of profile structure in selecting the best fitting model.

4.2.3.2. Step 2: identify predictor covariates to profile membership

A multinomial logistic regression was performed with Mplus 7 (Muthén & Muthén, 2012) to identify covariates that predicted profile membership and the odds ratios associated with their prediction. The purpose of this analysis was to compare high and low socialisation profiles against a normative group to determine which covariates were predictive of high or low profile membership. In this analysis, the semantics of 'normative' are purely statistical and carry no other context. Several covariates with a suspected relationship with socialisation were chosen for the regression based on supportive literature.

4.3. Results

Age (m=27.77 years (SD=4.91), range=15-45), neighbourhood quality (m=8.08 (SD=2.27), range=0-12), interpersonal sensitivity (m=89.68 (SD=16.33), range =36-144), and weighted adverse life events (m=3.8 events (SD=2.99), range=0-27) were used as continuous variables in this analysis. Categorical maternal variables are described in Table 4.1. The majority of this population fell into the upper 4 occupation levels (cumulative 62.6%) with the remaining 37.4% in the lower 3 levels. A small percent experienced discrimination (15.9%) and a smaller percentage experienced depression (9%). Home stability in this population was largely stable (cumulative 87.5%) compared to unstable (cumulative 12.5%). Individuals abused by a stranger (15.7%) and non-stranger (13.7) comprised less than a third of the sample, and 92.3% reported the presence of a partner.

Table 4.1. Population counts and percentages for maternal variables

	Population	Valid Percentage
Socioeconomic status		
Higher manager/admin/professional	657	5.9
Lower manager/admin/professional	2,696	24.2
Intermediate occupations	3,579	32.1
Small employers, own account workers	40	0.4
Lower supervisory and technical	286	2.6
Semi-routine occupations	2,367	21.3
Routine occupations	1,496	13.5
Missing	4,524	
TOTAL	15,645	100.0
Discrimination		
Yes	1,946	15.9
No	10,267	84.1
Missing	3,432	
TOTAL	15,645	100.0
Depression		
Yes	1,137	9.0
No	11,461	91.0
Missing	3,047	
TOTAL	15,645	100.0
Home stability		
Very stable	5,628	45.5
Fairly stable	5,203	42.0
Unstable	1,068	8.6
Very unstable	481	3.9
Missing	3,265	
TOTAL	15,645	100.0
Abuse		
Yes (stranger)	1,758	15.7
Yes (non-stranger)	1,533	13.7
No	7,937	70.7
Missing	4,417	
TOTAL	15,645	100.0
Presence of a partner		
Yes	7,348	92.3
No	612	7.7
Missing	7,685	
TOTAL	15,645	100.0

Table 4.2 shows the fit indices for the latent profile analysis of this population based on the 5 dimensions of the prenatal maternal social environment. The 3-group solution was selected as the best fit model based on the fit criteria. The AIC is lower than for a 2-group solution by a wide margin and while it continues to decrease while profiles increase, those decreases are negligible and the same is true for the BIC and SSABIC. The Lo-Mendel-Rubin's LRT shows that increasing models are not significantly better than the 3-group. Entropy drops from the 2-group to the 3-group but then decreases only slightly for the other models. Taken together, the 3-group solution is a strong choice for best fit but it was also the most parsimonious based on the thesis theme of examining mismatch between high and low socialisation phenotypical individuals.

Table 4.2. Fit indices for latent profile analysis

	AIC	BIC	SSABIC	LRT *(p)*	Entropy
2 class	132696.50	132815.49	132764.65	19182.24 (<0.01)	0.86
3 class	**126428.73**	**126592.36**	**126522.44**	**6170.78 (<0.01)**	**0.82**
4 class	123498.98	123707.23	123618.24	2890.70 (<0.01)	0.81
5 class	121075.36	121328.23	121220.18	2393.35 (<0.01)	0.81
6 class	119849.09	120146.58	120019.47	1216.78 (<0.01)	0.79
7 class	119003.78	119345.90	119199.71	842.43 (<0.01)	0.81
8 class	118044.10	118430.84	118265.59	954.81 (0.68)	0.80

AIC Akaike information criterion, *BIC* Bayesian information criterion, *SSABIC* sample size adjusted BIC, *LRT* Lo-Mendell-Rubin's adjusted likelihood ratio test

Figure 1 (below) shows the endorsement probability plot for the 3-group solution. The large High Socialisation endorsement group is described by consistent endorsement rates across the 5 dimensions, with Primary Support expectations slightly higher than Secondary Support. The moderately-sized normative Baseline Socialisation group falls a bit below the mean and mirrors the High group in consistency and support expectations. The small Low Socialisation group falls further below the mean and is described by higher rates of Secondary Support and

Contact, with the difference between Primary and Secondary Support being particularly notable.

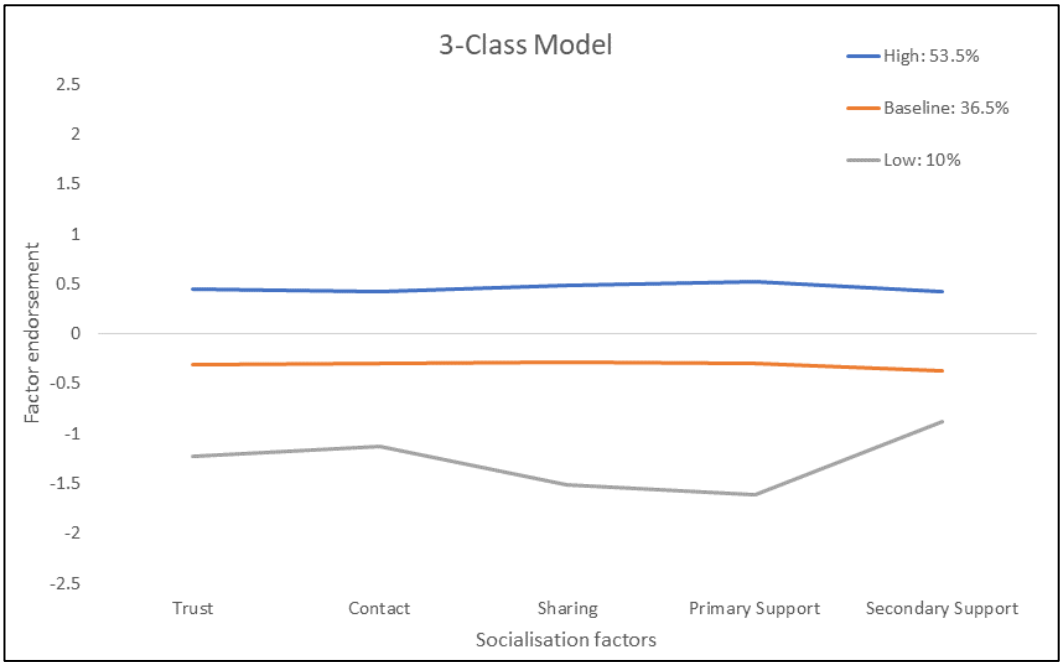

Figure 4.1. Endorsement probability plot for prenatal maternal social environment profiles

Figures 2-7 (below) detail the plots of the unselected models from the LCA. In all permutations of this model, the High profile remains stable across the 5 dimensions and comprises at least 30% or greater of the population. With each iteration, new Normative and Low profiles vary by dimension and size, dividing and sub-dividing into discreet profiles as the models grow in complexity.

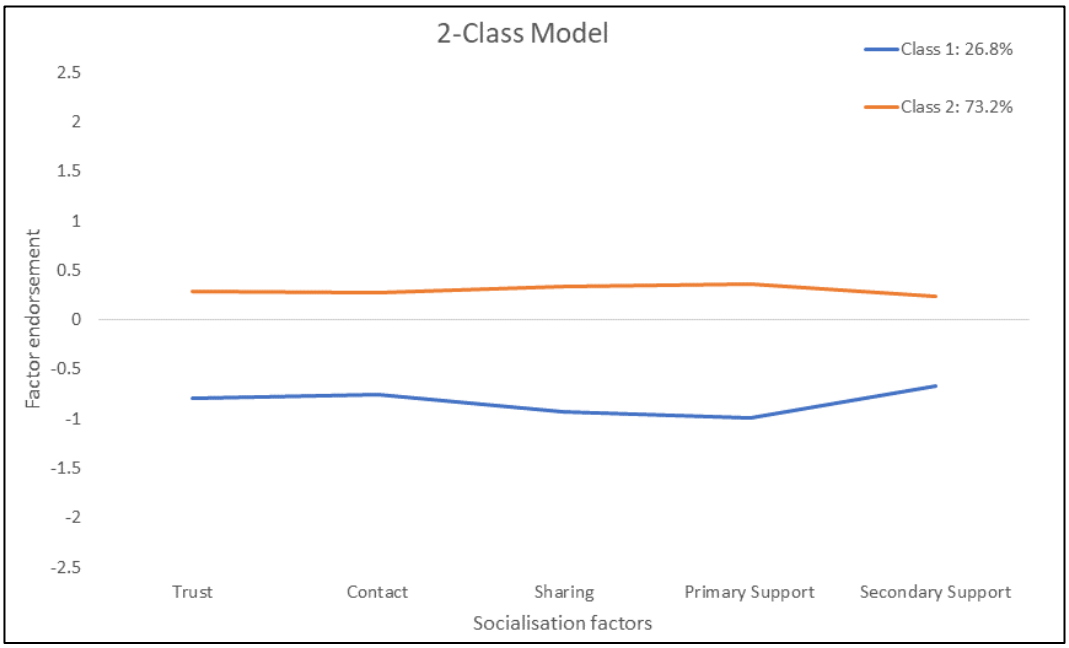

Figure 4.2. Endorsement probability plot for a 2-class model

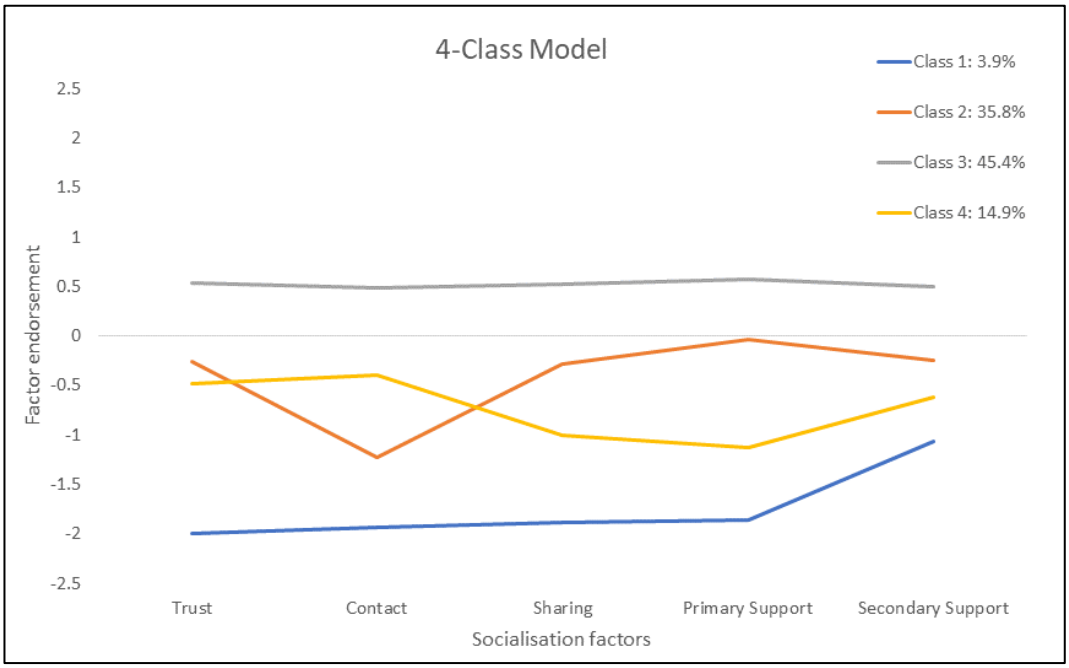

Figure 4.3. Endorsement probability plot for a 4-class model

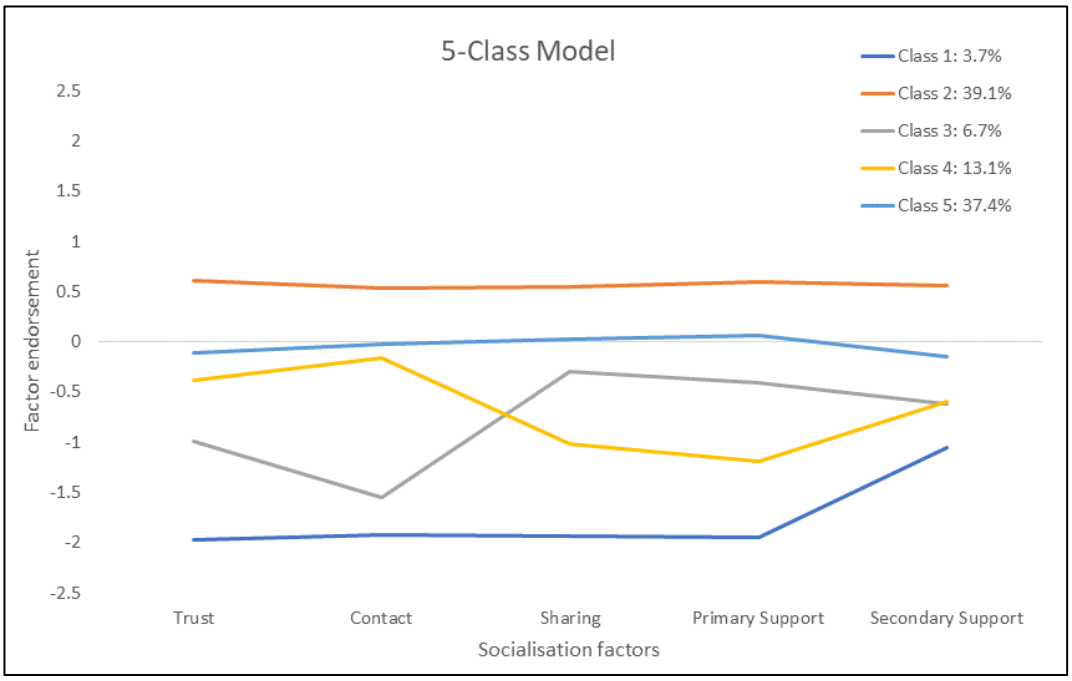

Figure 4.4. Endorsement probability plot for a 5-class model

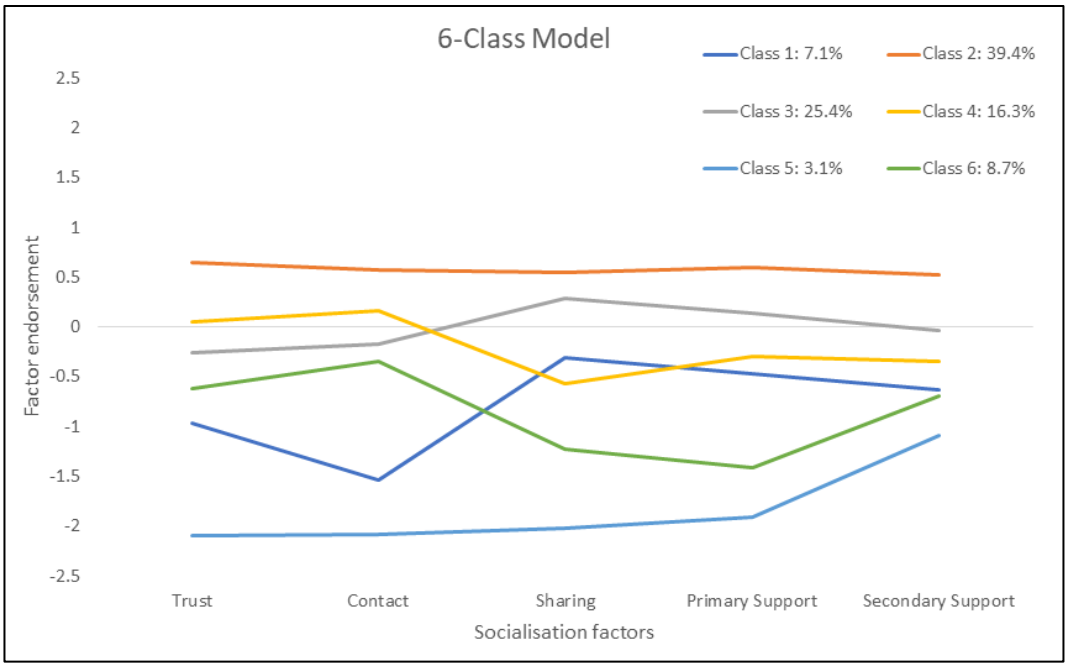

Figure 4.5. Endorsement probability plot for a 6-class model

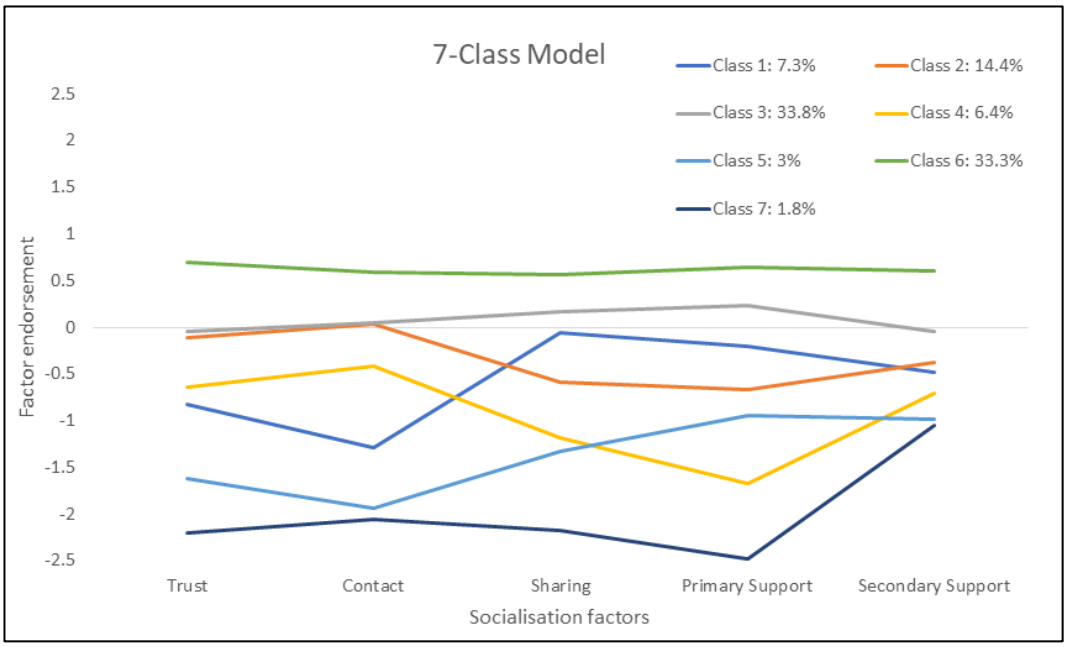

Figure 4.6. Endorsement probability plot for a 7-class model

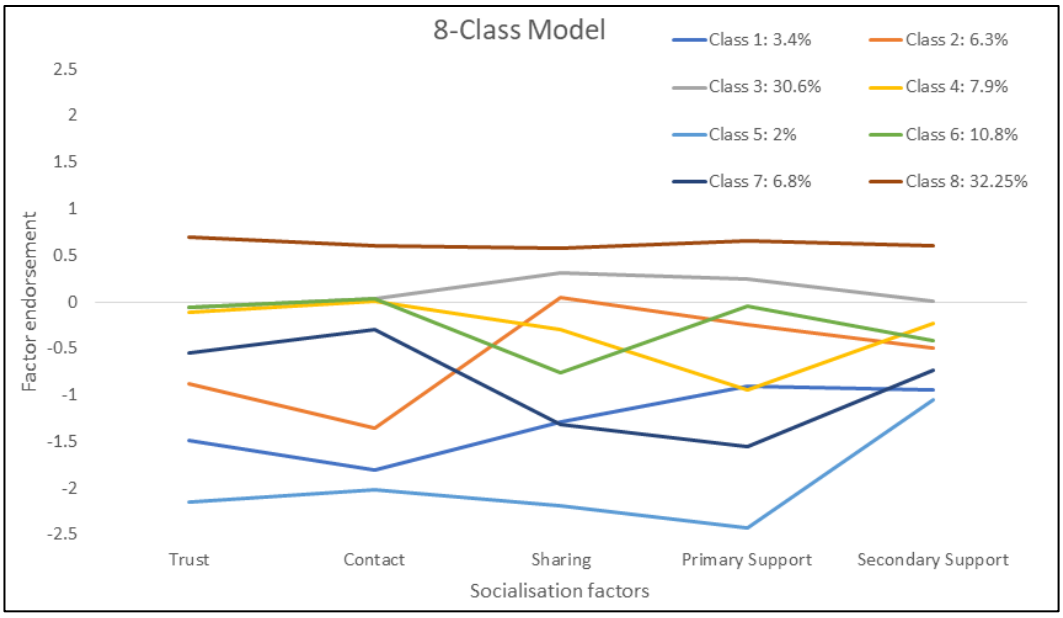

Figure 4.7. Endorsement probability plot for a 8-class model

A multinomial logistic regression was conducted to determine which covariates predicted High Socialisation or Low Socialisation profile membership when compared against the normative Baseline Socialisation profile. Table 4.3 (below) describes these results, including results using the High Socialisation profile as the reference group. In the Baseline Socialisation reference model, age, home instability, and abuse (by both stranger and non-stranger) were not significant predictors. The High Socialisation profile was described by higher SES,

neighbourhood quality, interpersonal sensitivity score, life events, and presence of a partner. The Low Socialisation profile was described by higher SES, neighbourhood quality, life events, and the presence of discrimination and depression. In the High Socialisation reference model, age and abuse (by both stranger and non-stranger) were not significant predictors. The Baseline Socialisation profile was described by SES, neighbourhood quality, interpersonal sensitivity, and life events. The Low Socialisation profile was described by SES, neighbourhood quality, interpersonal sensitivity, life events, discrimination, depression, home instability, and absence of a partner.

Table 4.3. Covariate predictors of socialisation profile membership

	Odds ratio (95% confidence intervals)			
	High Soc. Ref. Baseline	Low Soc. Ref. Baseline	Baseline Soc. Ref. High	Low Soc. Ref. High
Age	1.01 (.99-1.01)	1.00 (.98-1.02)	0.98 (.97-1.00)	0.98 (.97-1.00)
SES	**0.92*** (.89-.95)**	**1.14*** (1.09-1.19)**	**1.08*** (1.04-1.11)**	**1.23*** (1.18-1.29)**
Neighbourhood Quality	**1.04*** (1.02-1.05)**	**0.97** (.96-.99)**	**0.96*** (.94-.97)**	**0.93*** (.92-.95)**
Interpersonal Sensitivity	**0.98*** (.98-.99)**	1.00 (.99-1.01)	**1.01*** (1.00-1.01)**	**1.01*** (1.00-1.02)**
Life Events	**0.98*** (.97-.98)**	**1.02*** (1.01-1.03)**	**1.02*** (1.01-1.03)**	**1.05*** (1.03-1.06)**
Discrimination	1.13 (1.00-1.29)	**0.88** (.82-.95)**	0.87 (.77-.99)	**0.78*** (.68-.88)**
Depression	1.26 (.99-1.61)	**0.45*** (.35-.58)**	0.79 (.61-1.01)	**0.35*** (.27-.46)**
Home Instability	1.33 (.78-2.26)	0.63 (.33-1.21)	0.74 (.44-1.27)	**0.47** (.24-.90)**
Abuse Stranger	0.99 (.85-1.16)	1.02 (.81-1.28)	1.00 (.86-1.17)	1.02 (.82-1.27)
Abuse Non-Stranger	0.93 (.78-1.11)	1.25 (1.00-1.56)	1.06 (.89-1.26)	1.33 (1.08-1.65)
Partner	**0.75** (.60-.94)**	1.38 (1.05-1.83)	1.32 (1.06-1.65)	**1.84** (1.41-2.40)**

*p<0.05; **p<0.01; ***p<0.001

4.4. Discussion

4.4.1. Latent Class Division

The series of LPAs run during this phase of analysis examined models from a 2-group through 8-group solution, though not every model was a meaningful or statistically valid fit for the underlying profile structure of the data. In evaluating the fit indices for this series of analyses, the 3-group model combined the best statistical fit with the main aim of the thesis hypothesis, to compare high and low socialisation. Having proposed an effect (epigenetic changes to offspring based on prenatal maternal social isolation) evident in specific circumstances (a 'mismatch' in preferred social environments in adolescence), the most salient way to examine this effect was in the 'extremes'. Therefore, choosing the 3-group model meant analyses based on 2 groups diverging in opposite directions from a 'normative' group, making it possible to compare these groups both to the baseline group and to each other.

The High socialisation class was the largest at 53.5% of the population and was typified by a consistent endorsement (0.42 to 0.52) across all 5 dimensions of the prenatal maternal social environment. Examined in depth, this group showed marginal dips in *Contact* compared to *Trust* and *Sharing*, and in *Secondary Support* compared to *Primary Support*. The High class should not be thought of as 'over-socialised' but that group mean endorsement of these factors fell over the model mean. The model described this class as consistent in socialisation. These were women enjoying mutually trusting relationships with frequent contact where they felt comfortable sharing, reassured that if difficulties arose, they had ample support from their close circle but lesser so from acquaintances.

The normative Baseline class was the second largest at 36.5% and was described by stable endorsement (-0.37 to -0.28) through the 5 factors presented in the model. As with the High group, *Primary Support* expectations were marginally higher than *Secondary Support*. This group fell below the model mean of zero but should not be considered in deficit nor as an example of 'normative' socialisation. Rather, the Baseline class was the closest to the mean for this population. Here, the

model showed a group with similarly consistent socialisation and the certainty of more support from friends/family than associates. The main difference between the Baseline and High classes was where they fell compared to the mean, making their delta the amount of socialisation i.e., the extent of item endorsement.

The Low socialisation class was the smallest at only 10% and dimensional endorsement showed variation in the 5 dimensions (-0.88 to -1.61), all of which were lower than the other 2 classes. This group was described by higher *Contact* than *Trust* or *Sharing*, with *Primary Support* being the lowest endorsed factor and *Secondary Support* being the highest. As there was no universally accepted standard for the 'appropriate' level of socialisation, the Low class should not be thought of as 'under-socialised' but only falling the furthest below the mean in this population. As portrayed by the model, this was a group who still had interpersonal contact but were less likely to trust or share and who had greater expectations of support from acquaintances than from friends or family.

4.4.2. Covariate Predictors

Using a bank of chosen covariates, it was possible to determine which were significant predictors of profile membership. These covariates were selected based on the background literature supporting each one's link with socialisation, positive or negative. Predictor covariates with statistical significance in this model should not be taken as casual factors for high or low socialisation. Rather, they indicate the likelihood that a given individual would have item endorsements placing them in a specific group when examined in context to the group falling closest to the mean. For example, such an analysis could indicate if, when compared to the Baseline profile, were the members of the High and Low Socialisation profiles more likely to be older, younger, or was there no appreciable difference? In addition, a regression was performed with the High Socialisation profile as the reference group, highlighting the differences between the High and Low Socialisation profiles.

Compared against the normative Baseline group, membership in the High Socialisation group was predicted by a higher SES, higher neighbourhood quality,

lower interpersonal sensitivity, fewer adverse life events, and the presence of a partner. It is important to note these factors were what predicted a respondent would be categorised as belonging to the High Socialisation profile rather than the Baseline profile.

As SES increased, so increased the likelihood of an individual being a member of the High socialisation profile. This potentially reflected the financial independence to socialise freely in social venues (restaurants, clubs, bars, entertainment venues, etc.) rather than the budgetary constraints of a lower SES. There is also evidence of SES self-segregation and homogeneity in friend groups (Brown, 1981; Chan & Goldthorpe, 2004; in same-ethnic friendships, Smith, 2018). In tandem with SES, higher individual perception of neighbourhood quality was also a predictor of membership in the High socialisation profile. This was an expected result due to the likelihood that respondents with a higher SES would be more financially able to settle in an area meeting their desired standards. A neighbourhood that feels safe, attractive, and prosperous can foster increased well-being in its inhabitants (Carp & Carp, 1982). Increased neighbour social interaction is associated with less neighbourhood crime (Bellair, 1997) and feeling positively about one's neighbourhood contributes to positive physical and mental health (Connerly & Marans, 1985; Greenberg, 1999). Experiencing fewer adverse life events since becoming pregnant was another significant predictor for this profile, as increased rates of trauma correlate with reduced socialisation (Feldman & Vengrober, 2011).

A lower rate of interpersonal sensitivity (IS) was also a significant predictor of High Socialisation profile membership. IS was an aggregate of 5 related constructs: interpersonal awareness, need for approval, separation anxiety, timidity, and fragile inner-self. As discussed above, the IPSM correlates with the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1964), particularly with the neuroticism dimension, and is a reliable measure of internalised difficulties relating to and interacting with others. It would seem obvious that lacking difficulties socialising would predict a higher level of socialising but lower IS described a group confident interacting with others, not socially hyper-aware/vigilant, comfortable with variance in relationship intimacy and boundaries, who predominantly found validation in themselves rather than others. Harb, Heimberg, Fresco, Schneier, and

Liebowitz (2002) found the IPSM to be a "*valid and reliable*" tool for assessing social anxiety while Vidyanidhi and Sudhir (2009) found IS to be a defining factor between a social phobia sample and community control. In addition to desire for and ease of socialisation, low IS rates may have made members of this profile more desirable to socialise with. An individual who is hyper-sensitive, 'clingy', or needs constant validation from others requires more effort to socialise with than others may be willing to expend (Starr & Davila, 2008).

The presence of a partner also predicted High socialisation profile membership, showing a beneficial effect on participant socialisation. An obvious contributor to this may simply be more social opportunities available to the respondent between her social circle and that of her partner. Network overlap of social circles or a development of a larger, mutual social group is common in romantic partnerships (Stein, 2018). Romantic relationships and friendships can be self-fulfilling circles, whereby friend/family approval of the partner reinforces the individual's commitment or feeling they have made the right choice (Felmlee, 2001; Plamondon & Lachance-Grzela, 2018) and the romantic relationship provides a secure base and safe haven that then applies to friends/family (Asano & Yoshida, 2011). Another factor may be that with a partner to share the workload of daily life (especially if cohabitating and/or already parents), respondents had more free time/energy to devote to socialising.

The predictor covariates present a picture of this profile as 'well-off'; financially (higher SES and neighbourhood quality), emotionally (lower interpersonal sensitivity and fewer adverse life events), and practically (the presence of a partner). Taken together, these covariates created an environment that facilitated high levels of socialisation along the dimensions of *Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support* and describe group of women who possessed the multidisciplinary means to be able to successfully seek out and enjoy socialisation.

When compared to the normative Baseline group, membership in the Low Socialisation group was predicted by lower SES, lower neighbourhood quality, more adverse life events, discrimination, and depression. When compared to the High Socialisation group, membership in the Low Socialisation group was predicted by

lower SES, lower neighbourhood quality, higher interpersonal sensitivity, more adverse life events, discrimination, depression, home instability, and the absence of a partner.

Reflecting the High Socialisation profile, the Low Socialisation profile was described by SES, neighbourhood quality, and adverse life events, though on the other ends of those spectrums. This was a group with lower affluence than the Baseline group, residence in worse neighbourhoods, and a who endured a greater number of adverse life events, all of which are associated with lower rates of socialisation. Lower SES does show a negative impact on mental/physical health (Baum, Garofalo, & Yali, 1999; Blakey, Hales, & Woodward, 2004; Nandi, Glymour, & Subramanian, 2014), which in turn affects relationships with others, but it also limits mobility. Working a lower SES occupation means more work hours per week and a less flexible schedule in addition to less money to devote to 'frivolities' like socialising. SES also correlates with neighbourhood quality (Drukker, Feron, & van Os, 2004) and an individual living in a poor quality, unsafe area may not feel safe socialising within that neighbourhood or traversing in/out of it to socialise. There is also evidence to suggest that lower neighbourhood quality has a negative effect on physical health, mental health, and well-being (Connerly & Marans, 1985; Greenberg, 1999; Parkes, Kearns, & Atkinson, 2002).

Members of the Low Socialisation profile were likely to have suffered more adverse life events (traumatic events). Trauma is a complicated construct; easily downplayed ("Everyone has problems."), unrecognised ("It wasn't like I fought in a war."), or misappropriated ("I tripped in front of a crowd of people and was absolutely traumatised."). The truth is that much of the global population has undergone events at some point in life that constitute trauma (Kessler et al., 2017) even if they fail to recognise them as such. Major life events, while not often considered as trauma by the individual, can still prove stressful enough to have a profound effect. Adverse life events in the ALSPAC scale included death/severe illness (family, friends, self), separation/divorce, job loss, and domestic abuse, but also major life events, such as marriage, a new job, or moving to a new house (the scale was mostly 'negative' with 36 such items, 5 major life event items, and 1 'anything not on this list' item). There is an overwhelming body of research

concerning the associations between trauma and mental illness (Mueser et al., 1998; Houston, Shevlin, Adamson, & Murphy, 2010), poor health outcomes (Friedman & Schnurr, 1995; Krause, Shaw, & Cairney, 2004) and all-cause mortality (Boscarino, 2006; Hendrickson, Neylan, Na, Regan, Zhang, & Cohen, 2013; Elliot, Turiano, Infurna, Lachman, & Chapman, 2018).

Discrimination also significantly predicted membership in the Low Socialisation profile. Respondents indicated if they had experienced any instances of discrimination in the past year (on the basis of sex, skin colour/ethnicity, clothing, family background, speech/accent, religion, or 'any other reason not mentioned'). Despite the passing of the Race Relations Act 1976 (repealed and replaced by the Equality Act 2010), discrimination by ethnicity/national origin (Blackaby, Leslie, Murphy, & O'Leary, 1998; Maxwell, 2009; Zschirnt & Ruedin, 2016) was endemic in the UK during the 1990s. This was also true of discrimination based on religion (Hepple & Choudhury, 2001), disability (Barnes, 1995; Hyde, 1998), SES (Bradshaw, 2000; Ford, 2016), and sexuality/gender (Sargeant, 2009; MacLeavy, 2011) during that decade (Hepple, Coussey, & Choudhury, 2000). Ethnic demographics were not sourced for this thesis as epigenetic effects are catalyst dependant with universality, though as previous discussed, the first wave of ALSPAC mothers were predominantly white (Fraser et al., 2013).

It is well known and accepted that the experience of discrimination contributes to poor physical health outcomes (Williams, 1999; Mays, Cochran, & Barnes, 2007). In a meta-analysis of 134 populations, Pascoe and Richman (2009), found a significant negative relationship between the perception of discrimination and both physical and mental health outcomes. These experiences raised stress responses which were positively correlated with unhealthy behaviours and negatively correlated with healthy behaviours (Pascoe & Richman, 2009). A wealth of research has tied perceived all-cause discrimination to negative mental health outcomes (Kessler, Mickelson, & Williams, 1999; Mays & Cochran, 2001; Carter, Lau, Johnson, & Kirkinis, 2017), and specifically to social isolation (Oxman-Martinez et al., 2012; Negi, 2013). The experience of discrimination based on one's existence as a minority (racial, religious, economic, gender-based, or ability-based) constitutes trauma (Pieterse, Carter, Evans, & Walter, 2010; Williams, Printz, &

DeLapp, 2018), with all the excess ‘baggage’ trauma brings. The experience of discrimination can force one away from others out of lack of trust or not understanding the issue (Negi, 2013), and out of fear of being continued victimisation (Oxman-Martinez et al., 2012).

The experience of depression was the highest unique predictor of Low Socialisation profile membership. Most importantly, this item was phrased as ‘have you ever had severe depression?’ rather than ‘have you ever been diagnosed with severe depression?’ This distinction was important as it focused on occurrence of the experience, inclusive to those who may have experienced depression but avoided seeking diagnosis (or had been misdiagnosed/diagnosed with a covalent condition). The word ‘severe’ made a substantial difference as well; over 264 million globally have experienced some form of depression (World Health Organization, 2020) and that number was estimated at 172 million in 1990 (Liu, He, Yang, Feng, Zhao, & Lyu, in press). Not only did this designation cut out transient depressive episodes and sub-clinical experiences, it also forced a self-evaluation on the participant who then categorised their experiences with depression as ‘severe’.

Depression has been described in many ways by service users in language designed to convey its depths to the uninitiated. In qualitative studies, individuals have described a deteriorating mental state as “*spiralling down*” (McCann, Lubman, & Clark, 2012; Staneva, Bogossian, & Wittkowski, 2015), or related the experience to water via metaphors of “*drowning, sinking, crashing waves*” (Mallinson & Popay, 2007), even experiencing depression as a “*following shadow*” (Brown, Scales, Beever, Rickards, Rowley, & O’Dea, 2012). Such language clearly describes the suffering inherent in the symptoms. As discussed above, depression is defined by clinical indicators including low mood, lack of pleasure or interest in most things, fatigue, poor self-confidence, and feelings of guilt or self-blame. The Low Socialisation profile was predicted by ‘severe’ depression, indicating that some or all of these symptoms were potentially quite debilitating.

In a qualitative study of patient experiences, Kelly et al. (2011) found that constructs such as “*loneliness, interpersonal alienation, interpersonal conflict, and social withdrawal and isolation*” were the highest endorsed of all themes in the

study. It is not hard to imagine that individuals who are suffering from severe depression may pull back from others but also that historical severe depression leaves its mark. In a meta-analysis of long-term social functioning following a depressive episode, Kennedy, Foy, Sherazi, McDonough, and McKeon (2007) found that social limitation continued, and that lingering symptomology could contribute to this effect. In addition, while social support is beneficial in recovery from depression (Lyons, Perrotta, & Hancher-Kvam, 1988; Brugha, Bebbington, MacCarthy, Sturt, Wykes, & Potter, 1990) lower levels of social emotional support predicted a resurgence in symptomology (Nasser & Overholser, 2005), and seeking social support had associated disadvantages including stigma, insufficient support, and burden on the friend/relationship (Griffiths, Crisp, Barney, & Reid, 2011). In this sample, the experience of severe depression negatively affected the Low Socialisation profile and occurred in concert with increased adverse life events and experiences of discrimination.

The adverse life events and discrimination queried were 'since becoming pregnant' and did not constitute historical trauma while the depression item covered the respondent's life thus far. When taken together, the picture of the Low Socialisation profile becomes one of 'poorly-off' individuals (lower SES and neighbourhood quality) with a history of severe depression who suffered adverse life events and discrimination during the first 12 to 32 weeks of pregnancy. They may have already been living in isolation/low socialisation conditions by choice and persisted, reacted to their trauma by reducing socialisation, or had been in these conditions already due to depression or present environmental factors. Compared against the High Socialisation profile, the Low Socialisation profile was typified by higher IS, childhood home instability, and the absence of a partner. As members of the Low Socialisation profile had a higher expectation of support from acquaintances than friends/family, these results constitute a 'perfect storm' of psychosocial factors resulting in isolation. Regardless of unique individual circumstances, for the purposes of this thesis they had become the metaphorical exemplar prehistoric woman; pregnant and all alone.

4.4.3. Model discussion

With the prenatal maternal social environment defined, this phase of the analysis illustrated how members of the ALSPAC maternal cohort existed in and interacted with that environment. Utilising both a latent analysis and logistical regression, it was possible to create a unique picture of the sub-populations within the main study population as well as a more nuanced understanding of these profiles on an intimate level. Analysis here found 3 profiles: a High Socialisation profile (53.5%) described by higher, consistent endorsement of *Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support* and defined by overall higher SES and neighbourhood quality, presence of a partner, lower interpersonal sensitivity, and a higher number of adverse life events; a normative Baseline Socialisation profile (36.5%) described by consistent socialisation dimensions falling closest to the population mean; and a Low Socialisation profile (10%) described by the lowest endorsements of the dimensions (specifically *Sharing* and *Primary Support*) and defined by overall lower SES, neighbourhood quality, increased adverse life events, a history of severe depression, and experiences of discrimination.

Returning briefly to the over-arching themes at the foundation of this thesis, the High Socialisation and normative Baseline Socialisation profiles could be considered the closest to the assumed hominid/early Homo Sapiens societal experience, covariates notwithstanding. The Low Socialisation profile would approximate the individual in dangerous isolation, an outlier outcast from a social species through design or circumstance. Based on the percentage split by group in this population, the majority of the population was not in social isolation during the first trimester. Physical isolation would have been a veritable death sentence for humanity's ancestors, especially before the advent of settled habitation and agriculture, and it is possible that social isolation may have been just as dangerous in terms of individual survival. While both the hypothetical prehistoric mother in isolation and the mothers of the Low Socialisation profile were doubtlessly doing all they could to protect and ensure survival for their unborn child, it was hypothesised that cortisol was setting epigenetic processes in motion towards a similar goal.

4.4.4. Limitations

While increasing understanding of socialisation in this population, the results of these analyses must be taken in light of their limitations. Cases with missing data were dropped from this analysis, resulting in a 20% attrition (N=3,086). The remaining sample (N=12,549) was suitably robust for the analyses performed here (Tein, Coxe, & Cham, 2013) but less missing data may have provided a more complete picture of the study population. Covariates were chosen based on existent literature but were far from an exhaustive list of all possible covariates ALSPAC collected. Time and resources were the prevailing factors in covariate choice and given unlimited supplies of each, additional covariates would have been sourced in a hierarchical model to test proximity effects and control for potential confounders. Specifically, physical health measures (disability, chronic illness, obesity), additional environmental factors (education, household population) and personal factors (political alignment, IQ, religious belief, substance use/abuse) would be of interest in an aggregate model. As true as it ever was, the results of this analysis cannot be generalised further than the population cohort and while the ALSPAC cohort is comparable to the general UK population (Golding et al., 2001), replication studies for the main findings would be advised.

4.4.5. Impact and implications

While a simplistic model of profile specificity was expected based on supporting literature, contemporary expectant mothers' experiences will vary. The implications of these analyses spoke to identification and classification, which could prove useful in the GP or OBGYN's office during the 1st trimester. Understanding deficit environments and the factors that predict them can translate into preventative programs to lessen the effect of the deficit or even eliminate it entirely. Medical or physical intervention programs such as increasing folic acid intake (Rofail, Colligs, Abetz, Lindemann, & Maguire, 2011), alcohol/tobacco cessation (Room, Babor, & Rehm, 2005; Bell, Salmon, Bowers, Bell, & McCullough, 2010), and prenatal nutrition (Barker, 1998) have proven successful. Mental health and social interventions designed to prevent isolation could also prove effective. These

programs could start in the GP's office with identification and assessment, following with interventions geared towards the severity of the deficit, for example, information on local expectant mother groups or women's groups in the community. If there are significant isolation or mental well-being issues, further referral to mental health professionals would be important to address not just the isolation but other underlying problems. Such protocols would be crucial for the mother and offspring by addressing her well-being while also reducing the chances of foetal epigenetic modification due to isolation.

4.4.6. Conclusions

Due to the rich nuance in this data not directly related to the main hypotheses here, these analyses will be revisited in future work. With greater time and resources, there is value in exploring this population along these dimensions, specifically broadening what causal historic variables to apply. In addition, replication trials in similarly sized populations and in differing cultures would be able to determine if the effects here are cultural or universal. With the prenatal maternal social environment modelled, profiles identified and described by predictor covariates, the next step was to 'fast forward' and focus on the offspring population in its late childhood/early adolescence. Having suggested that the maternal social environment created phenotypic differences, the next phase of analysis would model the offspring social environment to determine how correctly the children's genomes had anticipated the need for social survival.

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Chapter 5

Modelling the childhood social environment

5.1. Study Introduction

In the last chapter, a latent profile analysis was used to determine socialisation profiles in the ALSPAC maternal cohort (High, Baseline, and Low) and a logistic regression was used to identify what covariates described those groups. Having defined the prenatal socialisation levels of the mothers, the next step was to determine if the prenatal maternal social environment had an effect on the offspring cohort. As with the mothers, it was important to first model the childhood social environment as an analytical foundation to understanding socialisation in the child cohort. ALSPAC's methodology was rigorous and provided a wealth of data to examine child socialisation, both in questionnaire responses from the mother concerning the child and from the children themselves. These data would be used to determine an underlying structure to the child social environment and potentially identify any indicator covariates associated with it.

Inheritors of a proposed social phenotype, the ALSPAC child cohort were born, grew through the postnatal period, early childhood, and in this chapter, had entered middle childhood. This phase of the analysis utilised child self-completed data collected when the cohort was approximately 9.5 years old. With the World Health Organisation (2014) defining adolescence as beginning at age 10, this age was chosen specifically to get a 'snapshot' of the child social environment before the transition into adolescence. It was hypothesised that differing social environments would mean a difference in psychopathology dependant on the prenatal maternal social environment and moderated by the child social environment. Modelling socialisation in the child cohort, as in the maternal cohort, created a conceptual model describing the social environment, but also fit into the overall process in this work of examining the relationship between these 2 environments and child psychopathology.

5.1.1. Socialisation in middle childhood

'Middle' childhood is defined as the ages 6 to 12 years (Collins, 1984). The World Health Organization (2014) considers adolescence to be the developmental

period spanning from ages 10 to 19, but most lay definitions consider childhood ending at the onset of puberty, which varies by individual difference. With the developmental explosion of early childhood concluded, the brain enters an environmentally influenced phase of neural growth and refinement (Mah & Ford-Jones, 2012). It is also a transitional time of cognitive, emotional, and psychosocial development as the child gains more independence and personal agency. Their social environment broadens and social mobility increases. The end point, adolescence, will mark the beginning of the next developmental phase, as the sphere of individual identity influence shifts from parents/family to predominantly peers/friends (Tanti, Stukas, Halloran, & Foddy, 2011).

Brain development in middle childhood is an ongoing process of growth, improvement, and refinement with increased rates of synaptic pruning (Edin, Macoveanu, Olesen, Tegnér, & Klingberg, 2007; Karbach & Unger, 2014). Physical coordination improves alongside physiological maturation (Lopes, Rodrigues, Maia, & Malina, 2011; Lloyd, Oliver, Faigenbaum, Myer, & De Ste Croix, 2014). Cognitive skills and executive functioning improve, as does processing speed and working memory (Luna, Garver, Urban, Lazar, & Sweeny, 2004) as brain volume increases in specific regions (Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008), best described as cognitive 'growth spurts' (Somsen, van't Klooster, van der Molen, van Leeuwen, & Licht, 1997). Plasticity increases during these sensitive periods of development and learning (Knudsen, 2004), informing behaviour, and will reach its height during adolescence (Fuhrmann, Knoll, & Blakemore, 2015). It has been proposed that middle childhood evolved as a developmental stage in humans, as it is non-existent in other primates (Thompson & Nelson, 2011), to allow for greater social learning and development (Bogin, 2006) due to the significant maturation of social skills during this period (Berry & O'Connor, 2010). The foundations of socialisation formed in early childhood during the crucial phase of social brain development mature as brain regions responsible for social cognition and evaluation also mature (Nelson & Guyer, 2011; Mills, Lalonde, Clasen, Geidd, & Blakemore, 2012), particularly the medial prefrontal cortex (MPFC, van Noordt & Segalowitz, 2012; Somerville, Jones, Ruberry, Dyke, Glover, & Casey, 2013).

Child social development in early childhood is dominated by 2 processes, emotional self-regulation and theory of mind, which also mature and refine during middle childhood. Emotional self-regulation requires the social cognition to first evaluate the situation, then to predict various outcomes, and finally to act appropriately, regulating any conflicting emotions (Hoffman & Russ, 2012) and acting within social norms (Zeman, Cassano, Perry-Parrish, & Stegall, 2006). Theory of mind is a cognitive ability allowing an individual to attribute knowledge, motivations, beliefs, and emotional states to others, acknowledging that others have minds of their own (Gallagher & Frith, 2003). This developmental milestone is considered universal and is present in most neurotypical children by age 4-5 (Wellman & Liu, 2004). Understanding that another person has agency of their own facilitates predictive social cognition and environmental evaluation, both critical to emotional self-regulation and ultimately to socialisation (Cole, Dennis, Smith-Simon, & Cohen, 2009).

Peer socialisation in early childhood is largely adult-directed and often adult-supervised (Coley & Hoffman, 1996), meaning that the peer social groups of young children are either ones of convenience (siblings, cousins, neighbour children) or without child choice (assigned classroom, children of their parents' friends, arranged playdates). Children normally lack the mobility that defines adult socialisation, but social interactions become less supervised during middle childhood, which grants increased choice and individual agency in social relationships. Middle childhood marks the beginning of a shift in influence from parents/family to peers, a process that will continue through adolescence, when the individual's social network will become predominantly non-family (Laursen & Williams, 1997). Adapting to and functioning withing these broader social environments is a crucial part of social development during middle childhood (McHale, Dariotis, & Kauh, 2003). Peer evaluation becomes more important to social identity (Rodkin, Ryan, Jamison, & Wilson, 2013) in both dyadic friendships and the wider system of peer groups/environments (Franco & Levitt, 1998), with social competence and prosocial behaviour increasing social status, making entry into both interpersonal and group relationships more fluid (Cillessen & Bellmore, 2002).

Group dynamics become more important to socialisation during middle childhood. Children as young as age 5 have displayed group member self-identification and group status awareness (Nesdale & Flesser, 2001; Bennett & Sani, 2011) with cognitive antecedents likely present earlier (Bennett & Sani, 2008). The drive to be accepted is evolutionary in nature, tied to survival by group (Bowles, 2006; Hare, 2017), but the want to feel accepted by the group can be considered a 'security' need per Maslow (1943) and is a fundamental motivation (Baumeister & Leary, 1995). Status matters in this environment as a low-status child accepted into a higher status group gains the benefit of increased socialisation and social mobility (Tajfel, 1974; Levine & Moreland, 1994), a child 'falls from grace' within a group and is rejected, or an entire group suffers a loss of status. The group social mechanisms of in-group favouritism can be beneficial to the child's self-esteem, self-confidence, and identity (Bigler, Jones, & Lobliner, 1997; Pugh & Hart, 1999), while peer acceptance can be as important as individual friendships (Parker & Asher, 1993). Interpersonal acceptance/rejection has been found to be intertwined with intergroup acceptance/rejection (Killen, Mulvey, & Hitti, 2013) in the middle childhood social environment, meaning social risks can pay both interpersonal and intergroup dividends.

5.1.2. Social isolation in middle childhood

Social risk does not always yield a reward and the consequences of poor prosocial behaviour and/or social failure are not pleasant. Children may socially withdraw voluntarily, fearing the rejection or ostracism of social failure, or as a result of these processes (Rubin, Coplan, & Bowker, 2009), leading to social isolation. Distress from psychopathology, particularly depression (Nolen-Hoeksema, Girgus, & Seligman, 1992; Gullone, Ollendick, & King, 2006), may also cause the child to pull back from social interaction in a cycle of symptomology and isolation (Boivin, Poulin, & Vitaro, 1994). Involuntary isolation is considered to be peer-driven (Ladd, 1999), assuming that if a child is not self-isolating, they desire social interaction. Rubin and Mills (1988) found 2 types of isolated child in a longitudinal sample (N=77): passive isolated and active-immature. Both were consequences of peer rejection and the former showing passive internalising behaviours and the later

more unpredictable externalising behaviours. The dichotomy was also found in a longitudinal sample (N=87) by Hymel, Rubin, Rowden, and LeMare (1990, pp. 2019), who refer to social isolation as "*a risk factor in early development*." Regardless of the pathway to social isolation, its effects are still detrimental to the child from both a developmental and psychopathological perspective (Rubin, Hymel, Mills, & Rose-Krasnor, 1991).

Bullying constitutes a specific form of forced social isolation (Spriggs, Iannotti, Nansel, & Haynie, 2007; Wang, Nansel, & Iannotti, 2011), incorporating an additional level of psychological trauma (Tehrani, 2004; Lutgen-Sandvik, 2008; Penning, Bhagwanjee, & Govender, 2010). A cross-sectional study of bullying in 40 countries (N=202,056) found prevalence rates of 8.6% - 45.2% in boys and 4.8% - 35.8% in girls (Craig et al., 2009). Bullies are often victims themselves (Ma, 2001; Unnever, 2005), and both being bullied and bullying are associated with increased psychopathology risk (Kelleher, Harley, Lynch, Arseneault, Fitzpatrick, & Cannon, 2008; Gibbs, Horwood, & Fergusson, 2011; Benedict, Vivier, & Gjelsvik, 2014). While the impact of bullying/peer victimisation is clear from the vast body of literature available, is it only within the past 2 decades that policymakers have identified it as a significant public health issue (Srabstein & Leventhal, 2010; Dale, Russell, & Wolke, 2014).

Rejection, whether self-initiated or the result of interpersonal/intergroup processes, is distressing due to the fundamental human need to belong. This distress is powerful enough to be identified via neural imaging during lab simulations of peer rejection (Crowley, Wu, Molfese, & Mayes, 2010; Eisenberger, Lieberman, & Williams, 2012). Increased local activation was seen in the brains of chronically rejected participants (Will, van Lier, Crone, & Güroğlu, 2015) which could be indicative of later desensitisation and potential mental health outcomes (Lambe, Craig, & Hollenstein, 2019). A sub-set of individuals are particularly sensitive/reactive to rejection, experiencing greater distress (Downey & Feldman, 1996; Masten et al., 2009) which is linked to reduced gray matter volume (Sun et al., 2014) and is correlated with anxious/depressive symptomology (Silk, Siegel, Lee, Nelson, Stroud, & Dahl, 2014; Heeren et al., 2017). Importantly, the neural systems involved in processing rejection develop throughout middle childhood and into

adolescence (Bolling, Pitskel, Deen, Crowley, Mayes, & Pelphrey, 2011), with self-regulation moderating rejection distress (Trentacosta & Shaw, 2009; McCain, Younginer, & Elledge, 2020) and social competence abilities reducing the risk of psychopathological behaviours (Hoglund, Lalonde, & Leadbeater, 2008).

Social support is also a powerful mediator of rejection distress and the stress of social isolation, both in lab simulated rejection (Morese, Lamm, Bosco, Valentini, & Silani, 2019) and in lived experience (Parker & Asher, 1993; Peters, Riksen-Walraven, Cillessen, & de Weerth, 2011). If social isolation is considered a deficit environment, with the rejected/isolated child metaphorically 'starving' for contact, it does stand to reason that even the smallest instance of social support or the most tenuous of friendships can alleviate some of the burden. Returning to the proposed social phenotype hypothesis, a child primed for (and potentially acclimated to) a highly social environment and craving external sources of arousal could become especially 'starved' in isolation. Morese, Lamm, Bosco, Valentini, and Silani (2019) suggest that as isolation is the absence of a fundamental need tied to survival, the 'social pain' of rejection can be read as a physiological call to action. This warning to seek homeostasis is similar to loneliness, hunger, and thirst.

Mental and physical health outcomes of rejection and social isolation in children mirror those in adults, particularly an increased risk of psychopathological symptomology and full diagnosis (Rubin & Coplan, 2007; Oh, Rubin, Bowker, Booth-LaForce, Rose-Krasnor, & Laursen, 2008) during middle childhood. In adolescence, social isolation increases the risk of psychopathology (Hall-Lande, Eisenberg, Christenson, & Neumark-Sztainer, 2007), alcohol/substance abuse (French, Conrad, & Turner, 1995; Prinstein & La Greca, 2004), and suicidality (King & Merchant, 2008; Endo et al., 2017). While social isolation in middle childhood and adolescence is no guarantee of isolation in adulthood, the severity of the experience constitutes trauma (Hoover, 2015), with all the additional mental and physical outcomes of childhood trauma (Almquist, 2011; Mock & Arai, 2011). Whether due to self-selection isolation or rejection/peer victimisation, the state of social isolation in middle childhood produces distress above and beyond its contributory factors, with effects that can persist past childhood (Caspi, Harrington, Moffitt, Milne, & Poulton, 2006; Lacey, Kumari, & Bartley, 2014).

5.1.3. Maternal influences on the childhood social environment

The previous 2 chapters were structured around defining how the maternal cohort socialised during pregnancy and what in their lives influenced that socialisation. While the primary hypothesis concerned offspring psychopathology outcomes in adolescence, it was also realistic that the prenatal maternal social environment and/or the predictor covariates which contributed to it affected the child social environment. Exploring these covariates and their relationships with this environment was an important part of the analytical model used during this phase. A later chapter will focus solely on controlling for several aspects of the postnatal environment, including covariates with psychosocial implications. For this analysis, 6 maternal covariates were chosen: maternal childhood home stability, neighbourhood quality, SES, the presence of a partner, and socialisation profile membership (High or Low).

Maternal home stability was the sole 'legacy' covariate used in this analysis, as the others were a part of the prenatal environment or classifications of that environment. Part of the 'adverse' covariate category in Chapter 3, maternal home stability was considered in the context of trauma, included due to the negative effect an unstable childhood home can have on adult mental health outcomes (Lizardi, Klein, Ouimette, Riso, Anderson, & Donaldson, 1995; Forrest & Riley, 2004). Maternal home instability was a significant difference between the Low and High Socialisation profiles, though not a defining covariate of either when compared to the normative Baseline profile. The adverse covariate category was potentially two-tailed, with the possibility for the absence of these traumas to have a positive effect on socialisation. It was included in this analysis due to the effects of maternal home stability on the mother which had the potential to extend to their offspring.

Those effects could come in several forms. An unstable childhood home constituted significant trauma which could affect the mother psychologically (formation of PTSD/CPTSD, poor mental health outcomes) and physiologically (heritable epigenetic modifications as per the transgenerational transmission of

trauma theory). The stability level of the home may have influenced the mother's attachment style with her own parents and informed her attachment style with her children, either positively or negatively. There exists a vast body of literature concerning attachment style, a theory describing the intimate relationship between mother and child (Bowlby, 1953; 1958), and how it can impact on childhood/adolescent friendships (Fraley & Davis, 1997; Rubin, Dwyer, Booth-LaForce, Kim, Burgess, & Rose-Krasnor, 2004), adult friendships (Bartholomew & Shaver, 1998), romantic relationships (Feeney & Noller, 1990; Feeney, 2008), and one's own relationship with one's children (Bifulco, Moran, Jacobs, & Bunn, 2009). It was also possible that home stability was part of a broader network of psychosocial variables affecting the mother and through this, her offspring, with home stability the most visible 'proxy'.

Neighbourhood quality and SES, two demographic maternal covariates, were also included in this analysis. There is an established relationship between them, as being of higher SES is correlated with living in a higher quality area with the reverse also being true (Yen & Kaplan, 1999; Wenden, Carpiano, & Robert, 2008; Hackman & Farah, 2009). Living in a low-quality area is associated with negative health outcomes (Wen, Hawkley, & Cacioppo, 2006) and increased distress for safety and security (Baba & Austin, 1989; Wang et al., 2019), constituting both subjective and objective stressors. Lower SES is also associated with negative health (Poulton et al., 2002; Cohen, Janicki-Deverts, Chen, & Matthews, 2010) and mental health outcomes (Saraceno & Barbui, 1997; Hudson, 2005), with financial strain associated with increased distress and other negative outcomes (Price, Choi, & Vinokur, 2002). It was very possible that between the prenatal period and late childhood, the family moved to a better area or the mother's SES increased; thus the use of these covariates in this analysis highlights their potential effect on the foetal genome, with postnatal control to feature in a later analysis.

The presence of a partner during the mother's pregnancy was one of the covariates that differentiated the High and Low Socialisation profiles. Individuals in the maternal cohort with a partner were more likely to be in the High Socialisation profile when compared against the normative Baseline profile, and those without a partner were more likely to be in the Low Socialisation profile when compared

against the High profile. This was noteworthy from a purely epigenetic viewpoint, i.e., objective/subjective stresses of being pregnant without a partner could affect the foetal genome. When taken together with Low Socialisation profile mothers also being of lower SES and living in poorer quality neighbourhoods compared to the other groups, the lack of support from a partner would be keenly felt, especially after the child's birth. It is reasonable to assume that many of the maternal cohort without partners during the prenatal period later entered into relationships, thus this covariate was included in an epigenetic context as a specific type stressor during pregnancy.

Membership in the High or Low Socialisation profiles was considered as an indicator covariate in this analytical model. It was possible that epigenetic priming had affected the offspring, leading to children of High Socialisation mothers seeking out and enjoying socialisation while children of Low Socialisation mothers avoided or had difficulty socialising. An association between profile and environment may have been present but explained by contributory covariates to the prenatal maternal social environment. It was also possible that the maternal social profile had no effect on the child social environment but only became a factor if the offspring was in a mismatch social environment in adolescence. As this analysis was exploratory in nature, maternal social profile membership was included as it was theorised to show an effect.

5.1.4. Childhood covariates and the social environment

The gender of the study child was used in this exploratory model as a potential covariate indicator. Participation in a gendered society results in generalised gender roles being passed on to young children, primarily by their parents (Witt, 1997) who may do so unintentionally (Eccles, Jacobs, & Harold, 1990). While there is no universal difference in socialisation between the genders, gendered social behaviour does differ in broad trends, with popularity/social desirability of children tied to these traits (Adler, Kless, & Adler, 1992). While not a lynchpin of the overarching hypothesis, there was the possibility for a gender effect and so it was included in this phase of the analysis.

Adverse life events (specifically being taken into care, physical abuse, and sexual abuse) were also included as child-based covariates. Data was present at 1.5, 2.5, 3.5, 5, 6, 7, and 8.5 years of age, covering the postnatal period through early to late childhood. Childhood trauma is a main casual factor in the development of child post-traumatic stress disorder (PTSD; World Health Organization, 1992) and has been implicated in poor physical health outcomes (Goodwin & Stein, 2004; Maschi, Baer, Morrissey, & Moreno, 2013; De Bellis & Zisk, 2014) and increased risk of substance abuse (Mulvihill, 2005). An extensive body of literature exists exploring the effects of childhood trauma on relationships (Wolfe, Wekerle, Scott, Straatman, & Grasley, 2004; Rholes, Paetzold, & Kohn, 2016), including its association with isolation and loneliness (Shevlin, McElroy, & Murphy, 2015). Aside from overall psychopathology, trauma is associated with increased risk of depression (Heim, Newport, Mletzko, Miller, & Nemeroff, 2008), anxiety (Heim & Nemeroff, 2001), psychosis (Read, 1997; Read, van Os, Morrison, & Ross, 2005), and overall psychopathology (Copeland et al., 2018). It is also well established that early adverse life events can interfere with normal cognitive development during brain growth (Perry, Pollard, Blakley, Baker, & Vigilante, 1995; van der Kolk, 2003), including disruption in the medial prefrontal cortex, responsible for social judgement and evaluation.

Childhood trauma can have a lasting impact. Trauma affects the individual in the immediate aftermath of the event as well as influencing outcomes later on in life. A child traumatised due to adverse life events may withdraw from their peers (Hattori, 2006), experience negative self-evaluation (Soler, Paretilla, Kirchner, & Forns, 2012), have difficulties with emotional self-regulation (Shields & Cicchetti, 2001; Kinniburgh, Blaustein, Spinazzola, & van der Kolk, 2005), or develop antisocial coping mechanisms (Thompson & Calkins, 1996; Garnefski, Kraaji, & Spinhoven, 2001). Examining these events across childhood, from 18 months to 8.5 years, meant also being able to explore a temporal effect should trauma be a covariate indicator of the child social environment. Given the extent of the damage that adverse life events can cause across the lifespan and all of which negatively impacting socialisation, it was important to include these data when modelling the child social environment.

5.1.6. Study aims

As it was proposed that the prenatal maternal social environment could affect the offspring, a method was undertaken to test this hypothesis. The maternal phases of analysis began with modelling the environment, which was undertaken with the offspring portion of the project as well to ensure a strong foundation for additional analyses. The goal of this study was to utilise child self-report data to model the childhood social environment while identifying associations between indicator covariates and this structure. The model produced was a cross-sectional snapshot of the child social environment at a critical time, both in terms of the child cohort themselves and the developmental timeframe of this project. Defining the child social environment at age 9.5 years, at the later end of middle childhood but not yet adolescence, meant evaluating socialisation before the complications of adolescence set in. This avoided the flux state of pubertal hormones, peak developmental plasticity, and the rapid (though incomplete) development of the 'social brain' systems and structures (Blakemore, 2008, 2012). These elements would be confounding to any study of this nature but while using secondary data eliminated the design/collection work, it also sacrificed control, leaving insufficient data to properly test this specific hypothesis in adolescence. The timing of this model was also important considering the next phase, a longitudinal model of offspring psychopathology, using repeat measure data from ages 7 through 11 years. With a dimensional understanding of the child social environment at the midpoint of that span, it was possible to evaluate psychopathology trajectories in relation to socialisation.

In this analysis, an 8-item scale was used to model the child social environment and several maternal and child cohort covariates were included to test their impact as indicators/predictors of child socialisation. It was hypothesised this environment possessed an underlying structure which was influenced by the prenatal maternal social environment profile of the mother and other environment and individual covariates. An exploratory structural equation model (ESEM) was selected as an appropriate analytical framework for this phase of analysis. It allowed for flexibility in testing several measurement models while incorporating a structural

model for each iteration. Incorporating both analyses into one model preserved parsimony and reduced error. With a cross-sectional representation of socialisation in middle childhood established, the next step would be to determine its association with psychopathology between ages 7 and 11 years.

5.2. Methodology

5.2.1. Sample

The main population consisted of ALSPAC Children of the 90s offspring cohort (N=15,645) with cases with missing data excluded (N=4,181). Of the cohort sample, 49.69% were female, 96.09% were white, and 6.22% came from a low-income household (Boyd et al., 2012).

Data from the maternal cohort was also utilised (N=15,645; N=12,549 after missing data cases dropped). Mean age for this population was 27.77 years (SD=4.91 years) with a range of 15-45. Most respondents had lived in the Avon catchment area for at least a year: 53.4% had lived in/near Avon all their lives, 16.9% over 10 years, 11.2% between 5 and 9 years, 13.6% between 1 and 4 years, and 5% for under a year (Herrick, Golding, and the ALSPAC Study Team, 2008). The population was further described as 79.1% homeowners, 79.4% married, and 97.8% were white/Caucasian (Fraser et al., 2013).

5.2.2. Measures

Data used in this phase of the analysis included maternal self-complete information focused both on her and the child as well as self-complete information from the child.

5.2.2.1. Child-completed data

This analysis used 8 items from the first section of a child-completed survey. These items covered friends/friendship and were taken here to form a scale describing socialisation. Measure details and methodology are discussed in Chapter 2 (Section 2.5.3.1.)

5.2.2.2. Maternal covariates

Several maternal covariates were incorporated into this analysis, sourced from the mother-based self-complete prenatal questionnaires 'About Yourself' (12 weeks gestation), 'Having A Baby' (18 weeks gestation), and 'Your Pregnancy' (32 weeks gestation). These included the presence of a partner, SES, neighbourhood quality, and home stability. Complete methodologies for these covariates are available in Chapter 2 (Section 2.5.2.). Two covariates were derived variables from Chapter 3: membership in the High Socialisation profile and membership in the Low Socialisation profile.

5.2.2.3. Child covariates

Covariates which were child-based but completed by the study parent were used in this analysis. Full details and usage of these covariates is discussed in Chapter 2 (Section 2.5.3.1.).

5.2.3. Analytic strategy

An exploratory structural equation model (ESEM) was chosen as the best analysis technique to model the structure of the child social environment while, at the same time, the influence of covariates on this structure. ESEM combines the benefits of both exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) into a single technique with the 'freedom' of EFA and the methodological

strength of CFA (Tóth-Király, Bõthe, Rigó, & Orosz, 2017). This method allows for additional multivariate testing and regressions between factors and covariates within the same model while reducing systematic error (Asparouhov & Muthén, 2009). In some cases, performing an EFA to determine a latent structure and following with a secondary analysis testing associated variables is preferable, due to the restrictive nature of factor cross-loadings in CFA (Marsh, Morin, Parker, & Kaur, 2014). At other times, an EFA is preferable to an ESEM when exploring a structure and covariates without a implying a reciprocal relationship between them. This was the case in Chapter 2, where an EFA was used to model the prenatal maternal social environment, with those dimensions used to establish latent profiles within the population before a logistic regression of predictor variables was run. The interest was in how predictor covariates interacted with the latent profiles, not the dimensions of socialisation itself. It was decided to use an ESEM in this analysis as the goal was to model the social environment and its relationship with the chosen covariates. Exploratory structural equation models were tested with MPlus 7 (Muthén & Muthén, 2012) as described below.

5.2.3.1. Step 1: model the child social environment

The first stage was to determine the underlying structure of the child social environment using the 8 categorial items selected from the questionnaire ‘My Hands, My Feet, and Me’ given at 9.5 years. This was accomplished with a measurement model evaluating a 1 through 3-factor solution. A 4-factor model was attempted but was not able to run and the model did not terminate normally due to the limited number of items. The purpose of this step was to build a foundation for further analyses by modelling this environment’s latent dimensions.

As with the EFA performed in Chapter 2, goodness-of-fit is important in ESEM, and several fit indices are commonly used to evaluate the model. The chi-square (χ^2), Root Mean Square Error of Approximation (RMSEA; Steiger, 1990), Tucker-Lewis Index (TLI; Tucker & Lewis, 1973), Comparative Fit Index (CFI; Bentler, 1990), and the Standardised Root Mean Square Residual (SRMR) were used to compare models generated in this analysis. The chi-square value in a fitted model

should exceed 0.05 (Barrett, 2007) however, the chi-square is vulnerable to sample size at both extremes (Bentler & Bonett, 1980). The RMSEA is resilient to the effect sizes of a large sample and is parsimonious, acknowledging that even the best-fit model is only ever an approximation of reality (Chen, Curran, Bollen, Kirby, & Paxton, 2008). The TLI is a non-normed fit index (NNFI) that is also resilient to sample size and should range between 0 and 1 (Hu & Bentler, 1999) with a larger value indicating a better fit; typically from .95 (Cangur & Ercan, 2015). Likewise, the CFI, developed by Bentler (1990), accommodates for population in addition to comparing the covariance of the model against a null model (Hooper, Coughlan, & Mullen, 2008). As with the TLI, values are between 0 and 1 with .95 being a generally accepted threshold (Hu & Bentler, 1999). The SRMR is the standardised delta between the observed and expected correlations, a measure of fit resilient to sample size and a variety of confounding conditions (Maydeu-Olivares, Shi, & Rosseel, 2018). As an absolute measure with 0 being a total fit between the observed and expected, a value less than 0.08 indicates a good fit (Hu & Bentler, 1999). These fit indices were invaluable here due to the large population sample used.

In determining the fit of latent factors, several information criteria results were used to further compare models: the Akaike information criterion (AIC, Akaike, 1987), the Bayesian information criterion (BIC, Schwarz, 1978), and the sample size-adjusted Bayesian information criterion (SSABIC, Sclove, 1987). The AIC functions as a quality determinant for models against each other and while it cannot provide the absolute quality of any given model, it can inform on the best among models, providing a log likelihood. Related to the AIC, the BIC relies on Bayesian inference but is susceptible to sample size where the sample exceeds the number of parameters, thus the SSABIC can be used in tandem to correct for larger populations. The lower these indicators, the better the model fit.

5.2.3.2. Step 2: determine relationships between factors and indicators

The second part of the analysis was the structural component examining the relationship between the child social environment factors and the chosen covariate indicators. This analysis utilised 14 covariates with suspected relationships to the

child social environment based on supportive literature. The factors generated by the measurement component of each model being tested were regressed on the selected maternal and child covariates to identify covariate indicators with impact on a child's social environment as defined by the factors underlying that environment. Each 2-part model was run separately increasing from a unidimensional model to a 3-factor model.

5.3. Results

Respondent endorsements of each item in the friends section of the personal evaluation scale (Table 5.1) show a fairly stable sub-sample of missing replies ranging from 48.9% to 50.1% of the total population (N=15,645). The missing sub-sample includes blank responses, improper type responses, and responses of 'don't know'. While it is a substantial portion of the cohort, the responding population more than satisfied the 'rule of thumb' in sample size for factor analysis, with a sample >1000 classed as excellent for accurate results (Comrey & Lee, 1992).

Table 5.1. Population counts and percentages for socialisation scale item endorsement

	Response	Population	Valid Percentage
study child has lots of friends	Not true	168	2.1
	Mostly untrue	187	2.3
	Partly true	725	9.1
	Mostly true	1,329	16.6
	True	5,573	69.8
	Missing	7,663	
study child makes friends easily	Not true	371	4.7
	Mostly untrue	378	4.7
	Partly true	1,452	18.2
	Mostly true	2,105	26.4
	True	3,669	46.0
	Missing	7,670	
other kids have more friends than study child	Not true	3,129	39.5
	Mostly untrue	1,975	24.9
	Partly true	1,293	16.3
	Mostly true	654	8.3
	True	865	10.9
	Missing	7,729	
study child gets along easily with kids	Not true	199	2.5
	Mostly untrue	222	2.8
	Partly true	1,019	12.8
	Mostly true	2,285	28.6
	True	4,264	53.4
	Missing	7,656	
Other kids want study child to be their friend	Not true	363	4.7
	Mostly untrue	516	6.6
	Partly true	1,908	24.5
	Mostly true	2,091	26.9
	True	2,897	37.3
	Missing	7,870	
study child has more friends than most other kids	Not true	1,243	15.9
	Mostly untrue	1,062	13.6
	Partly true	2,295	29.4
	Mostly true	1,751	22.4
	True	1,449	18.6
	Missing	7,845	

Table 5.1. Population counts and percentages for socialisation scale item endorsement

study child is popular with kids of same age	Not true	317	4.0
	Mostly untrue	365	4.6
	Partly true	1,439	18.3
	Mostly true	2,045	25.9
	True	3,715	47.1
	Missing	7,764	
most other kids like study child	Not true	203	2.6
	Mostly untrue	228	2.9
	Partly true	1,340	17.1
	Mostly true	2,167	27.6
	True	3,912	49.8
	Missing	7,795	
	TOTAL	15,645	100.0

Neighbourhood quality (M=8.08 (SD=2.27), range=0-12), was used as a continuous variable. The non-trauma covariates are described in Table 5.2: SES, the presence of a partner, home stability, socialisation profile, and study child gender. Participants employed in intermediate occupations were the largest group (32.2%) with a majority of sample falling in the upper half of the measure (62.3%). Participants with partners comprised 92.3% of the valid sample. Mothers experiencing stable homes (87.5%) outnumbered unstable (12.5%), as did membership in the High Socialisation profile (81.8%) compared with membership in the Low Socialisation profile (18.2%). Gender was evenly distributed in the child cohort (52.1% male). Child adverse life events at ages 1.5, 2.5, 3.5, 5, 6, 7, and 8.5 years are described in Table 5.3, with experiences of trauma the lowest at age 1.5 years (2.6%) and ranging between 3.2% and 4% for the other time points.

Table 5.2. Population counts and percentages for non-trauma covariates

	Population	Valid Percentage
SES		
Higher manager/admin/professional	657	5.9
Lower manager/admin/professional	2,696	24.2
Intermediate occupations	3,579	32.2
Small employers, own account workers	40	0.4
Lower supervisory and technical	286	2.6
Semi-routine occupations	2,367	21.3
Routine occupations	1,496	13.5
Missing	4,524	
TOTAL	15,645	100.0
Partner presence		
Yes	7,348	92.3
No	612	7.7
Missing	7,685	
TOTAL	15,645	100.0
Home stability		
Very stable	5,628	45.5
Fairly stable	5,203	42.0
Unstable	1,068	8.6
Very unstable	481	3.9
Missing	3,265	
TOTAL	15,645	100.0
Socialisation profile		
High socialisation	3,200	81.8
Low socialisation	711	18.2
Missing	11,734	
TOTAL	15,645	100.0
Study child gender		
Male	7,699	51.2
Female	7,349	48.8
Missing	597	
TOTAL	15,645	100.0

Table 5.3. Population counts and percentages of child life events ages 1.5 – 8.5 years

	Population	Valid Percent
1.5 Years		
Yes	284	2.6
No	10,765	97.4
Missing	4,596	
TOTAL	15,645	100.0
2.5 Years		
Yes	406	4.0
No	9,833	96.0
Missing	5,406	
TOTAL	15,645	100.0
3.5 Years		
Yes	328	3.3
No	9,717	96.7
Missing	10,045	
TOTAL	15,645	100.0
5 Years		
Yes	376	4.0
No	9,067	96.0
Missing	6,202	
TOTAL	15,645	100.0
6 Years		
Yes	301	3.5
No	8,330	96.5
Missing	7,014	
TOTAL	15,645	100.0
7 Years		
Yes	266	3.2
No	8,176	96.8
Missing	7,203	
TOTAL	15,645	100.0
8.5 Years		
Yes	330	4.0
No	7,855	96.0
Missing	7,460	
TOTAL	15,645	100.0

Table 5.4 shows the fit indices for the measurement models of the ESEM. Indices for a unidimensional through 3-factor model are shown. The chi-square value decreased as each model increased in complexity and while it remained significant, it must be taken in conjunction with the other fit indices due to the large sample size (N=4,181) and the chi-square's known vulnerability to large samples. The RMSEA was less than 0.05 for all models and also steadily decreased. The TLI and CFI both increased, approaching 1 for the 3-factor model. Lastly, the SRMR was below 0.08 for all models, indicating good model fit (Hu & Bentler, 1999), and also decreased from the unidimensional to 3-factor model.

Table 5.4. Fit indices for exploratory measurement models

	χ^2	df	*p*	RMSEA	CFI	TLI	SRMR
1	**758**	**118**	**0.00*** **	**0.036**	**0.946**	**0.936**	**0.022**
2	325	97	0.00***	0.024	0.981	0.972	0.015
3	194	77	0.00***	0.019	0.990	0.982	0.011

*** *indicates significance at ≤0.001; best model in bold*

The information criteria results (Table 5.5) showed a decrease between the unidimensional and 2-factor model. However, moving from a 2 to 3-factor model provided only a negligible drop in AIC and SSABIC while the BIC increased.

Table 5.5. Information criteria for exploratory measurement models

	AIC	BIC	SSABIC
1	**86008.19**	**86249.05**	**86128.30**
2	85562.45	85936.41	85748.94
3	85446.09	85946.81	85695.78

AIC Akaike information criterion, *BIC* Bayesian information criterion, *SSABIC* sample size adjusted BIC; best model in bold

The unidimensional model (Table 5.6) showed moderate to strong factor loading scores across all items, ranging from 0.55 to 0.79. In the structural model (Table 5.7), only Maternal Home Stability (β = -0.104 (S.E.= 0.024)) and membership in the Maternal High Socialisation profile (β = 0.120 (S.E. = 0.036)) were significant indicators of the single factor underlying the child social environment in this model.

Table 5.6. Factor loadings for a unidimensional model

	Factor 1
has lots of friends	0.71
makes friends easily	0.70
other kids have more friends	-0.58
gets along easily with other kids	0.68
other kids want as a friend	0.70
has more friends than most other kids	0.55
popular with kids of the same age	0.72
most other kids like	0.79

Table 5.7. Covariate indicators in a unidimensional model

	Standardised Coefficient (S.E.) Factor 1
Maternal Home Stability	**-0.104*** (0.024)**
Neighbourhood Quality	0.003 (0.004)
SES	0.017 (0.009)
Partner	0.070 (0.069)
Gender (child)	0.040 (0.033)
Life Events (1.5 years)	0.016 (0.013)
Life Events (2.5 years)	-0.010 (0.009)
Life Events (3.5 years)	-0.004 (0.010)
Life Events (5 years)	-0.003 (0.010)
Life Events (6 years)	-0.015 (0.008)
Life Events (7 years)	0.004 (0.009)
Life Events (8.5 years)	-0.013 (0.007)
Maternal High Socialisation	**0.120** (0.036)**
Maternal Low Socialisation	-0.075 (0.063)

*p<0.05; **p<0.01; ***p<0.001

The 2-factor model (Table 5.8) returned moderate to high factor loading scores, ranging from -0.41 to 0.92, though the factors were highly correlated (0.83), raising issues of possible collinearity. In examining the structural model (Table 5.9), Maternal Home Stability (β = -0.086 (S.E.= 0.026)), Gender (β = 0.101 (S.E.= 0.036)), and membership in the Maternal High Socialisation profile (β = 0.152

(S.E.= 0.038)) were significant indicators of Factor 1. Maternal Home Stability (β = -0.108 (S.E.= 0.024)), SES (β = 0.022 (S.E.= 0.009)), Life Events at 6 years (β = -0.019 (S.E.= 0.008)), and membership in the Maternal High Socialisation profile (β = 0.090 (S.E.= 0.037)) were significant indicators of Factor 2.

Table 5.8. Factor loadings and correlations for a 2-factor model

	Factor 1	Factor 2
has lots of friends	**0.45**	0.28
makes friends easily	**0.78**	-0.01
other kids have more friends	**-0.41**	-0.19
gets along easily with other kids	**0.73**	0.01
other kids want as a friend	0.06	**0.65**
has more friends than most other kids	0.04	**0.52**
popular with kids of the same age	-0.17	**0.92**
most other kids like	0.01	**0.81**
Factor 1	1.000	
Factor 2	0.83	1.000

Table 5.9. Covariate indicators in a 2-factor model

	Standardised Co-Efficient (S.E.)	
	Factor 1	Factor 2
Maternal Home Stability	**-0.086** (0.026)**	**-0.108*** (0.024)**
Neighbourhood Quality	0.003 (0.004)	0.002 (0.004)
SES	0.005 (0.010)	**0.022** (0.009)**
Partner	0.090 (0.070)	0.057 (0.071)
Gender (child)	**0.101** (0.036)**	-0.001 (0.034)
Life Events (1.5 years)	0.014 (0.014)	0.016 (0.013)
Life Events (2.5 years)	-0.003 (0.010)	-0.013 (0.009)
Life Events (3.5 years)	-0.005 (0.011)	-0.003 (0.010)
Life Events (5 years)	0.00 (0.011)	-0.004 (0.010)
Life Events (6 years)	-0.004 (0.009)	**-0.019** (0.008)**
Life Events (7 years)	-0.008 (0.009)	0.011 (0.009)
Life Events (8.5 years)	-0.017 (0.008)	-0.009 (0.008)
Maternal High Socialisation	**0.152*** (0.038)**	**0.090** (0.037)**
Maternal Low Socialisation	-0.120 (0.068)	-0.040 (0.063)

*p<0.05; **p<0.01; ***p<0.001

The 3-factor model (Table 5.10), showed low to high factor loading scores, ranging from 0.31 to 0.83, with a high factor correlation between Factors 1 and 2, and moderately high correlations between Factors 1 and 3 and Factors 2 and 3. In the structural model (Table 5.11), Maternal Home Stability (β = -0.008 (S.E.= 0.028)), Gender (β = 0.096 (S.E.= 0.037)), and membership in the Maternal High Socialisation profile (β = 0.142 (S.E.= 0.040)) were significant indicators of Factor 1. Maternal Home Stability (β = -0.107 (S.E.= 0.025)) was the sole significant indicator of Factor 2. Maternal Home Stability (β = 0.081 (S.E.= 0.026)) and SES (β = 0.027 (S.E.= 0.011)) were both significant indicators of Factor 3.

Table 5.10. Factor loadings and correlations for a 3-factor model

	Factor 1	Factor 2	Factor 3
has lots of friends	**0.31**	0.25	-0.22
makes friends easily	**0.80**	-0.01	0.01
other kids have more friends	-0.01	0.01	**0.82**
gets along easily with other kids	**0.71**	0.03	-0.01
other kids want as a friend	0.12	**0.61**	0.01
has more friends than most other kids	-0.01	**0.47**	-0.12
popular with kids of the same age	-0.08	**0.83**	-0.01
most other kids like	0.07	**0.77**	0.02
Factor 1	1.000		
Factor 2	0.79	1.000	
Factor 3	-0.64	-0.62	1.000

Table 5.11. Covariate indicators in a 3-factor model

	Standardised Coefficient (S.E.)		
	Factor 1	Factor 2	Factor 3
Maternal Home Stability	**-0.0084****	**-0.107*****	**0.081****
	(0.028)	**(0.025)**	**(0.026)**
Neighbourhood Quality	0.002	0.001	-0.007
	(0.004)	(0.004)	(0.005)
SES	0.013	0.026	**0.027****
	(0.011)	(0.014)	**(0.011)**
Partner	0.102	0.056	-0.031
	(0.071)	(0.076)	(0.089)
Gender (child)	**0.096****	-0.013	-0.099
	(0.037)	(0.072)	(0.061)
Life Events (1.5 years)	0.010	0.015	-0.020
	(0.014)	(0.014)	(0.017)
Life Events (2.5 years)	-0.001	-0.014	0.007
	(0.010)	(0.010)	(0.012)
Life Events (3.5 years)	-0.003	-0.003	0.012
	(0.012)	(0.011)	(0.013)
Life Events (5 years)	0.000	-0.005	0.000
	(0.011)	(0.010)	(0.012)
Life Events (6 years)	-0.001	-0.020	0.016
	(0.009)	(0.010)	(0.014)
Life Events (7 years)	-0.010	0.012	-0.007
	(0.010)	(0.013)	(0.010)
Life Events (8.5 years)	-0.016	-0.008	0.010
	(0.008)	(0.010)	(0.015)
Maternal High Socialisation	**0.142*****	0.083	-0.121
	(0.040)	(0.064)	(0.112)
Maternal Low Socialisation	-0.113	-0.032	0.090
	(0.070)	(0.084)	(0.074)

*p<0.05; **p<0.01; ***p<0.001

Factor 1 was named Socialisation and was determined to have an indicative relationship with the covariates Maternal Home Stability and membership in the Maternal High Socialisation profile.

5.4. Discussion

5.4.1. Model selection and results

The analysis for this phase considered several possible models; a unidimensional, 2-factor, and 3-factor model. All 3 models met the criteria for statistical viability. While the 3-factor model showed the strongest fit indices, the difference between these and the results for the 2-factor model were not as great as between the unidimensional and 2-factor model, the factors were highly correlated (Floyd & Widaman, 1995), and they were of little contextual value. The factors of the 2-factor model were also highly correlated and while marginally contextually better than the 3-factor model, it was also rejected, and the unidimensional model was accepted as the model of best fit in describing the underlying structure of the child social environment and its covariate indicators. The factor loadings were moderate to high on a single factor labelled Socialisation. Maternal Home Stability (β = -0.104 (S.E.= 0.024)) and membership in the Maternal High Socialisation profile (β = 0.120 (S.E. = 0.036)) were significant covariate indicators of Socialisation, meaning the more stable the mother's childhood home life and/or the greater her prenatal socialisation, the more likely her offspring endorsed higher scores measuring their Socialisation.

The socialisation scale used in this analysis was the first use of child self-complete data in this project and hinged on the child's perception of themselves. Even the quantity themed questions relied on an estimation of the self against all others: 'has lots of friends', 'other kids have more friends', and 'has more friends than most other kids.' All 3 of these items were subjective, as 'lots' of friends might have been 4 for one child but 8 for another, and the comparison items required comprehensive social arithmetic. The desirability items ('other kids want as a friend', 'popular with kids of the same age', and 'most other kids like') involved self-evaluation of individual social worth and Theory of Mind in gauging how other children might view them. The ability items ('makes friends easily' and 'gets along easily with other kids') also dealt with a subjective topic (ease) and called for a child to define to themselves if they were 'making friends' and 'getting along' with others.

Whereas the prenatal maternal social scale was more concrete ('# of friends', '# of visits with friends in the past month', etc.), the child social scale was completely subjective and based solely on perception. While the possibility existed for respondents to commit Type 1 or 2 errors (over or underestimating their socialisation), the age of the sample may restrict these to outliers. By age 5, most children have acquired Theory of mind (Perner & Lang, 1999), though aspects of social cognition are present as early as 9 months (Carpenter, Nagell, Tomasello, Butterworth, & Moore, 1998), and Bigelow, Tesson, & Lewko (1992) found that children as young as 9 ascribed to a complex set of social 'rules' governing type and quality in friendships. The scale used here was given in Likert type format referring to how truly each statement described the child, but data was not collected on how the child felt about those descriptions. Some of the cohort may have already been in a mismatch social environment, primed for socialisation they were lacking or manifesting coping skills for non-existent isolation. However, it is important to note that the child social environment, like all environments, was not stable and very likely to change for each individual over time. It was modelled here as a 'starting point' at the gateway to adolescence and a baseline measure for the years that followed.

5.4.2. Covariate Indicators

Maternal Home Stability was a significant indicator of Socialisation in the unidimensional model describing the child social environment. While this maternal cohort covariate was not a significant predictor of the High Socialisation profile compared to the Baseline Socialisation profile, instability did differentiate the Low Socialisation profile when compared against the High Socialisation profile. Individuals in the Low Socialisation profile were more likely to come from unstable childhood homes than their highly socialised counterparts. Here, the children of mothers who grew up in more stable childhood homes had higher rates of Socialisation. This result must be considered in both directions; maternal childhood home stability produced an effect which positively affected offspring socialisation at age 9.5 years and maternal childhood home instability produced an effect which negatively affected offspring socialisation at the same age. It was also possible that

the ‘damage’ of instability was not present for the individuals raised in a stable home, and lack of this negative environment produced a positive result, rather than having an independent positive effect.

Growing up in an unstable home constitutes not only trauma, but a repeating continuum of trauma with lasting effects psychological effects. As discussed above, childhood trauma increases the risk of PTSD/CPTSD, anxiety, depression, psychosis, and substance abuse, which can all have a negative effect on child mental health, relationships, and socialisation. This is not to suggest that an unstable home yields an unstable person, rather that there are strong associations between home instability and the above risks. There also exists the possibility that this trauma left its mark on the maternal genome via epigenetic modifications to a hostile environment, manifesting as increased risk for PTSD (Yehuda & Bierer, 2007), early maladaptive schemas (Zeynel & Uzer, 2020) and other psychopathologies (Gröger et al., 2016). As children learn to socialise through understanding the emotions of others, even toddlers are able to pick up on their parents’ emotional states (Fox, 1989; Ursache, Blair, Stifter, & Voegtline, 2013), including the negative emotional fallout of their mother’s unstable home.

Another potential consideration with the maternal childhood home situation was its effects on the participant/child attachment style. Attachment theory describes the evolutionary-driven need for a child to form an intimate bond with a caregiver, usually its mother (Bowlby, 1953; 1958) and attachment style describes the 4 general patterns of behaviour quantifying that relationship (Ainsworth, Bell, & Stayton, 1971; 1974; Ainsworth, Blehar, Waters, & Wall 1978). Infants with secure attachment have confidence that their secure base (parent) will see to their needs and freely explore their environment, interacting with strangers. Infants who routinely do not have their needs met (or who have suffered abuse/neglect) manifest anxious-ambivalent and anxious-avoidant attachment styles, with negative affect and little consideration for the return of a parent from absence, where secure infants show pleasure. Disorganised attachment infants display strange distressed-based coping behaviours, sometimes seeming to disassociate, and this style was found almost exclusively in the children of mothers who had experienced trauma shortly before or

after the child's birth, including loss of a parent or a significant unresolved loss (Main & Hesse, 1993; Solomon & George, 2006).

More recently, attachment theorists have utilised aspects of neurodevelopment and gene-x-environment interactions to reconcile observed behavioural data with accepted developmental neuroscience (Fox & Hane, 2008). Attachment style can change in childhood/adolescence and adulthood due to a variety of influential factors (Davila, Burge, & Hammen, 1997; Jones et al., 2017) but remains relatively stable across the lifespan for most individuals (Fraley, 2002; Cozzarelli, Karafa, Collins, & Tagler, 2003). An individual's own attachment style also influences that of their child both directly and through mediators (Obegi, Morrison, & Shaver, 2004; Bifulco & Thomas, 2013; Cooke, Racine, Plamondon, Tough, & Madigan, 2019). Adults with non-secure attachment styles often have difficulties initialising and maintaining both romantic and platonic relationships (Feeney & Noller, 1990; Feeney, 2008) and are at an increased risk for psychopathology (Dozier, Stovall-McClough, & Albus, 2008; Mikulincer & Shaver, 2012) while secure attachment adults often enjoy fulfilling adult relationships (Pistole, 1989; Pascuzzo, Cyr, & Moss, 2013). Through attachment style, the stability of the maternal home in infancy/childhood may have produced lasting consequences for the participants and also for their offspring.

Additional psychosocial variables must be considered alongside trauma and attachment theory. Ecological systems theory (Bronfenbrenner, 1979) was cited earlier in reference to child social development but is also applicable when examining interactional relationships between psychosocial variables. Home stability can be seen as a potential indicator of systemic problems including poverty, poor social support, unmanageable health/mental health issues, and alcohol/substance abuse. A small amount of data was collected on the parents of the maternal cohort and their childhood demographic circumstances, making a full analysis of that childhood environment difficult.

Membership in the Maternal High Socialisation profile was also a significant indicator of Socialisation. Several of the covariate predictors of the High Socialisation profile were also included in the model but none had an independent

effect on Socialisation. As modelled in Chapter 3, this profile described a sub-group of the population cohort who were of higher SES, lived in higher quality neighbourhoods, had lower interpersonal sensitivity, fewer adverse life events, and had a partner. The aspects of this profile that were beneficial for socialisation in the maternal cohort were likely so for their offspring.

Children learn by imitation. Social modelling is the process by which a developing child imitates and replicates the behaviours they observe in others (Over and Carpenter, 2012), including a toddler's propensity to repeat a parent's favourite profanity. This process is not always positive, as a child observing a parent react with negative behaviour to a stimulus (for example, a spider), may unconsciously incorporate that behaviour as they age (an unexplainable fear of spiders). Nielsen, Simcock, and Jenkins (2008) suggest that social imitation serves a duel function of learning and social communication. Imitating the behaviour of a highly socialised mother would have the net benefit of increased social communication and social learning due to the increased contact. The Behaviourist model of learning focuses on behaviour and reward, theorising that positive behaviour which is rewarded is thus reinforced, becoming learned behaviour (Ertmer & Newby, 1993). It was not hard hypnotise a similar behavioural cycle: maternal social behaviour was imitated by the child, who was rewarded with social communication, attention, and praise, with social learning making the next social behaviour easier and the rewards acting as the impetus to do so. It has been well established children of parents who frequently socially engage with them during infancy show increased social, emotional, communication, and cognitive development (Landry, Smith, & Swank, 2006), increased by-word language acquisition (Golinkoff, Can, Soderstrom, & Hirsh-Pasek, 2015; Zhang et al., 2015), and higher verbal comprehension, vocabulary, and cognitive outcomes at ages 9-13 (Gilkerson et al, 2018).

Being the product of a stable childhood home and being a member of the maternal High Socialisation profile both influenced rates of Socialisation in the offspring cohort. While the rest of the chosen covariates were not significant indicators of the unidimensional child social environment, some (Neighbourhood Quality, SES, and the presence of a partner) were associated with membership in the maternal High Socialisation profile, making them tertiary influencer to the overall

temporal process. There is a clear interconnection of two-tailed covariates whereby those on the higher end benefit while those on the lower end suffer.

5.4.3. Limitations

The findings from this study must be viewed in light of the limitations present. Cases with missing data were dropped, reducing the sample size to N=4,181. Despite being substantially smaller than the original sample, it was still a robust sample size for this analysis, though the attrition was disappointing. The child social environment was modelled based on a single scale describing the child's perceptions of their quantity of friends, desirability as a friend, and ability to engage with others. If data had existed triangulating their perceptions with objective data from the mother and teachers on number of friends, frequency of interactions, etc., it would have helped create a much clearer picture of the child social environment. Having additional data from the child describing other aspects of their social environment would have been invaluable, as would having this scale repeated throughout childhood/adolescence for longitudinal modelling. Due to the temporal flow utilised in this thesis, the child social environment was modelled prior to controlling for the postnatal environment, which was concerned with the postnatal period's contribution to variance in later mental health outcomes. In addition, it must be mentioned that the results here may have been products of the era of data collection; the contemporary child social environment at age 9.5 years will differ due to cultural, socioeconomic, and technological changes in the ALSPAC catchment area.

If given the option for any available data, the inclusion of child and maternal physical health data would have been useful to examine the relationship between health and socialisation in middle childhood in the ALSPAC child cohort, as well as specific health variables such as child obesity or maternal smoking. If this study had been designed specifically to model the child social environment, more attitudinal data from the children on socialisation would have been helpful to facilitate a more complete exploration of this environment.

5.4.4. Impact and implications

Taken together, the results of this analysis are of a singular dimension, Socialisation, describing a child's perception of their social environment and relationship with it. This unidimensional construct was influenced by Maternal Home Stability in childhood and membership in the Maternal High Socialisation profile, covariates associated with other socioeconomic and life advantages. The purpose of this phase was to model and describe the child social environment as was done with the prenatal maternal social environment. The age chosen represented this environment at the end of childhood and before the social, emotional, and developmental upheaval of adolescence. It was necessary to have a representation of the child social environment before modelling change in socialisation and any adaptive psychopathology due to a mismatch environment in the years that followed.

The intent of research and its actual impact are often wildly different depending on popular understanding of the outcomes. That certain aspects of a mother's childhood and adult circumstances affect a child's socialisation is evident in the ALSPAC first wave population. As the analyses up to this point have shown, social environments are complex interactions between an individual, all other individuals, and innumerable influential covariates even before reaching concepts like situational context and societal norms. The implications of this analytical phase should not be taken as universal. That said, however, educators on both the class and system level should be aware of how a child's family/socioeconomic environments affect their peer socialisation. Schools in lower SES/poor neighbourhood quality areas are doubtless aware of the issues their students face but considering the implications of these factors on socialisation could help in forming programs to assist. As an example, when it was established that going without breakfast had a detrimental effect on learning and educational outcomes, a federal free breakfast program was launched in the United States in 1966, a mirror of the independent programs sponsored by the Black Panthers to benefit the children of lower SES families (Milkman, 2016). Screening at various points in childhood could also identify children with low socialisation and implement assistance programs.

5.4.5. Conclusions

The child social environment was modelled here as a baseline ‘snapshot’ of socialisation in the child cohort as they left childhood and entered adolescence, a crucial developmental phase. A sub-population of this cohort sample had gestated in a highly socialised prenatal maternal social environment while another sub-population gestated in a state of maternal isolation. It was hypothesised that difference had changed the genomes of the disadvantaged for survival in a sparce social environment, giving those individuals a distinct advantage in isolation over their highly socialised compatriots. It remained to test the main theory driving this project and determine the outcomes of the offspring cohort in a mismatched environment situation. Having modelled the prenatal maternal social environment, determined socialisation profiles existing within that environment with the predictors that defined those profiles, and modelled the child social environment with indicators of that environment, the next step was to longitudinally model adolescent psychopathology.

5.5. Chapter References

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Chapter 6

Modelling psychopathology across middle childhood

6.1. Study Introduction

Ultimately, this thesis aimed to explain psychological distress, therefore, a key component of the thesis was identifying how psychological distressed manifested in the cohort over time. Having modelled the child social environment (child social environment) in the previous chapter and established a 'snapshot' of the child cohort's experiences of socialisation during middle childhood, the next step was to model their mental health over time. In establishing a structural model of the prenatal maternal social environment (prenatal maternal social environment), identifying socialisation profiles in the maternal cohort, and modelling the child social environment, the cross-sectional data used was either contemporary (referring to the time of collection) or historical, in the case of several maternal variables. In this analysis, data was used longitudinally to establish a chronology of psychological distress through middle childhood. Data describing psychopathology from ages 7 to 11 years was used to model mental health trajectories in this cohort, with the cross-sectional model of the child social environment (identified in the previous chapter) falling mid-point, at 9.5 years. It was anticipated that psychopathology in this population would be described in terms of distinct trajectories over the 4 years examined, defined by latent classes in the population.

The assumption at this project's inception was that the prenatal maternal social environment contributed to a social phenotype with epigenetic processes as the actioning mechanism. Harsh conditions in the prenatal maternal social environment determined the type of environment offspring might expect and thus the adaptations in the genome would be specific to that type of environment with a goal of promoting survival. These adaptations were further hypothesised to be protective in nature, that a child born from a low socialisation prenatal maternal social environment would fare better in social isolation than one resultant of a high socialisation prenatal maternal social environment. It was also possible that a high socialisation phenotypical individual would fare better in a highly social environment than would their low socialisation counterpart. This effect was believed to be a combination of behaviours fitting the environment for which individuals were primed, and behaviours that were maladaptive outside of the expected environment. As an example, needing less interaction with others promotes survival in isolation

but could lead to overstimulation and distress in a highly social environment. Conversely, needing a great deal of interaction maintains wellbeing in that highly socialised environment but leads to increased distress in isolation. Thus, it was anticipated that the prenatal maternal social environment would affect the degree of distress at ages 9-11 years resultant of Socialisation at age 9.5 years.

It is important to note that no specific phenotype, genetic marker, or heritability estimate is a direct causal factor in human behaviour (Plomin & Rende, 1991; Plomin, DeFries, Knopik, & Neiderhiser, 2016). Behaviours are the result of a multifactorial system of contributory variables which are all context dependent from the large scale (societal norms, systems of belief) to the personal level (situation, life history, etc.) (Bronfenbrenner, 1979). The interaction between these factors drives behaviour, with hundreds of minor or confounding variables exerting influence on the individual, including the involvement of other people (Murray & Schaller, 2016). As previously discussed, many of the predictor or influencing factors should be thought of in terms of risk or likelihood of occurrence, especially in the context of a large population sample. However, the effect of the prenatal maternal social environment was predicted to be a significant contributor to the variance in behaviour in specific social environments, including the distress of environmental mismatch and resulting psychopathology. To test this effect, it was first necessary to model that psychopathology over time.

6.1.1. Psychopathology in middle childhood

Children may express their distress differently than adults but still suffer from many of the psychopathologies found in older populations (Belfer, 2008). A meta-analysis of 52 US and UK studies found that psychopathology prevalence in middle childhood populations to be 12% (Roberts, Attkisson, & Rosenblatt, 1998), mirrored by a later global meta-analysis of 41 studies from 27 countries which found prevalence rates of 13.4% for all disorders in children and adolescents (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). Onset age of psychopathology varies based on type of disorder (Kessler et al., 2007), environmental risk factors (Jaffee, Moffitt, Caspi, Fombonne, Poulton, & Martin, 2002), socioeconomic variables (Chen,

Matthews, & Boyce, 2002; Reiss, 2013), gender (Zahn-Waxler, Shirtcliff, & Marceau, 2008), and individual differences. While there is significant variation, most childhood onset disorders advent by ages 5 to 7 years (Merikangas, Nakamura, & Kessler, 2009; Polanczyk, Salum, Sugaya, Caye & Rohde, 2015), with exceptions being developmental disorders such as autism spectrum disorder, which is typically diagnosed within the first 5 years (World Health Organization, 2019). There is a significant increase in psychopathology onset during adolescence (Cicchetti & Rogosch, 2002; McGue & Iacono, 2005) and again in early adulthood, with those experiencing onset in middle childhood having an increased rate of lifetime prevalence (Kessler, Amminger, Aguilar-Gaxiola, Alonso, Lee, & Üstün, 2007; Kessler et al., 2007). It has been suggested that middle childhood is a confluence of period specific developmental vulnerabilities and multiple stressors, manifesting as distress and early psychopathology (Boyce et al., 2002; Zahn-Waxler, Shirtcliff, & Marceau, 2008).

Brain development in middle childhood has been described as a period of maturation and refinement, where the developmental explosion of early childhood is tempered through learning and experience (Luna, Garver, Urban, Lazar, & Sweeney, 2004; Mah & Ford-Jones, 2012). Plasticity and rates of synaptic pruning increase, resulting in greater neural flexibility (Knudsen, 2004; Lebel, Walker, Leemans, Phillips, & Beaulieu, 2008), though this process reaches its peak in adolescence. Problems during this sensitive period have the potential to derail normal brain development, leading to increased psychopathology risk in adolescence and adulthood (Grossman, Churchill, McKinney, Kodish, Otte, & Greenough, 2003; Belsky & de Haan, 2010), especially stress response over-stimulation of the HPA axis (Cicchetti & Curtis, 2015). HPA dysregulation has been implicated in childhood onset depression (Lopez-Duran, Kovacs, & George, 2009; Guerry & Hastings, 2011) and other affective disorders (Forbes, Williamson, Ryan, Birmaher, Axelson, & Dahl, 2006), adolescent depression (Van den Bergh, Van Calster, Smits, Van Huffel, & Lagae, 2007) and increased suicide risk (Braquehais, Picouto, Casas, & Sher, 2012; Giletta, Calhoun, Hastings, Rudolph, Nock, & Prinstein, 2015), and adult mental health outcomes (Mello, Faria, Mello, Carpenter, Tyrka, & Price, 2009). Childhood maltreatment and stress exposure is also associated with white matter irregularities and structural integrity issues (Teicher, Tomoda, & Andersen, 2006),

which are in turn associated with psychopathology risk (McCrory, De Brito, & Viding, 2010; Huang, Gundapuneedi, & Rao, 2012). In a longitudinal twin study, Chiang et al. (2011) found that environmental factors were the primary influencers on white matter development in middle childhood, with the gene x environment effect more influential than heredity.

Beyond brain physicality, middle childhood is a sensitive period for cognitive development. As discussed in Chapter 4, emotional self-regulation undergoes significant maturation over this period. While important to socialisation and interaction, emotional self-regulation is a mechanism which plays a vital role in adjustment (Lengua, 2003; Eisenberg, Spinrad, & Eggum, 2010), sensitivity to rejection (Ayduk, Mendoza-Denton, Mischel, Downey, Peake, & Rodriguez, 2000), and is a stabilising factor mediating the detrimental effects of hostile environments (Crespo, Trentacosta, Udo-Inyang, Northerner, Chaudhry, & Williams, 2019). Self-regulation is also important in the development of coping skills, additional mediators to stressors and adverse life events (Blair, 2010; Johnson, Perry, Hostinar, & Gunnar, 2019). Several environmental and socioeconomic factors can negatively affect the developmental process, specifically the multifactorial impact of poverty (Brooks-Gunn & Duncan, 1997; Hair, Hanson, Wolfe, & Pollak, 2015) and malnutrition (Martorell, 1999). Poorly developed emotional self-regulation is associated with behavioural issues in middle childhood (Trentacosta & Shaw, 2009), externalising symptomology (White, Jarrett, & Ollendick, 2012), and an increased risk of psychopathology in both adolescence and adulthood (Baker & Hoerger, 2012).

A child's identity and sense of individual agency also matures over middle childhood. As an infant, their identity was tied to their mother or primary caregiver with a separation occurring in early childhood as they began to assert their will. Erikson's psychosocial stages (1963, 1968) conceptualise this shift in identity throughout life and middle childhood marks the beginning of the identity formation process, which will enter a crucial phase in adolescence (Crocetti, Rubini, Luyckx, & Meeus, 2008; Meeus, van de Schoot, Keijsers, Schwartz, & Branje, 2010). Personal identity is a function of self-understanding which is fundamental to mental health and wellbeing, and crucial to self-worth, self-confidence, and self-evaluation (Thoits, 2013). Individual identity descriptors shift away from pure self-evaluation

and begin to incorporate the perception and evaluation of others into the evolving self-concept (Harter, 2006). Trauma at this stage of development can disrupt identity formation (Lawson & Quinn, 2013), with abuse, sexual abuse, and neglect being particularly damaging to a child's identity (Saha, Chung, & Thorne, 2011) if they asses themselves as deserving of or somehow causing the abuse (Harter, 2006). Identity difficulties in middle childhood can lead to attachment and socialisation issues in adolescence and beyond (Bailey, Moran, & Pederson, 2007).

In the inter-relational model of psychopathology in middle childhood, several psychosocial and chronic environmental stressors are known contributors to risk (Grant, Compas, Stuhlmacher, Thurm, McMahon, & Halpert, 2003). Lower SES constitutes a significant stressor on the family (Wadsworth & Berger, 2006), can be a barrier to proper care and intervention (Chow, Jaffee, & Snowden, 2003), and can mean inadequate access to nutrition to meet children's developmental needs (McLaughlin et al., 2012). Poverty has been associated with increased risk of psychopathology in childhood in longitudinal studies (Velez, Johnson, & Cohen, 1989; Costello, Compton, Keeler, & Angold, 2003), and there is an additional association between poverty and trauma (Hughes et al., 2017). As above, an unstable family home can contribute significant stress/trauma and an adverse home environment is also associated with increased psychopathology risk. This risk can come from a variety of factors, from the deliberate acts of abuse/neglect and domestic violence (Sanders & Becker-Lausen, 1995; Levendosky, Huth-Bocks, Semel, & Shapiro, 2002), to the unintended consequences of a parent dealing with mental illness (Stallard, Norman, Huline-Dickens, Salter, & Cribb, 2004; Reupert & Maybery, 2010), long-term health problems (Steele, Forehand, & Armistead, 1997), or substance abuse (Osborne & Berger, 2009). Finally, existing as an ethnic or social minority also contributes to overall risk of psychopathology during middle childhood (Steinhausen, 1987; Costello & Janiszewski, 1990).

Social factors during middle childhood can both contribute to psychopathology risk and serve as mediators to its effects. As previously discussed, peer rejection, exclusion, or ostracism constitute significant stressors (Williams, 2007; Masten et al., 2009) associated with both negative mental health (Sebastian, Viding, Williams, & Blakemore, 2010) and physical health outcomes (Almquist,

2009). The trauma of bullying can also be devastating to a child's wellbeing (Kelleher, Harley, Lynch, Arseneault, Fitzpatrick, & Cannon, 2008; Gibb, Horwood, & Fergusson, 2011; Benedict, Vivier, & Gjelsvik, 2014). Conversely, individual friendships and friend networks can mediate the negative effects of childhood stressors (Ueno, 2005; Bond, Butler, Thomas, Carlin, Glover, Bowes, & Patton, 2007; Rose, Carlson, & Waller, 2007) with a direct correlation between friendships and lower blood cortisol (Peters, Riksen-Walraven, Cillessen, & de Weerth, 2011). Higher peer status and peer recognition has also been associated with higher rates of mental wellbeing (Östberg, 2003). Self-regulation and other facets of social competence are factors in both successful socialisation and the development of coping abilities in middle childhood (Hoglund, Lalonde, & Leadbeater, 2008; Trentacosta & Shaw, 2009), potentially contributing to resilience.

When risk becomes reality, the stigma surrounding mental distress and mental illness is a significant roadblock to recovery, frequently resulting in secondary trauma and in some cases delaying intervention (Clement et al., 2015). A child experiencing mental distress may face stigma from their peers or educators (O'Driscoll, Heary, Hennessey, McKeague, 2012; Parcesepe & Cabassa, 2013; Kaushik, Kostaki, & Kyriakopoulos, 2016), resulting in further distress and isolation (Corrigan, Rafacz, & Rüsch, 2011). Self-stigma, or distress over their mental illness, is also a factor in loss of self-esteem and self-efficacy (Corrigan, Watson, & Barr, 2006; Mukolo, Heflinger, & Wallston, 2010), and may also affect the child's identity. Even without stigma, many psychopathologies are associated with social withdrawal in children/adolescents (Rubin, Coplan, & Bowker, 2009), specifically, depressive disorders (Boivin, Hymel, Bukowski, 1995; Katz, Conway, Hammen, Brennan, & Najman, 2011), anxiety disorders (Biggs, Vernberg, & Wu, 2012; Jakobsen, Horwood, & Fergusson, 2012), and psychosis (McClellan & McCurry, 1999), removing avenues of potential support. The child's family may react negatively to their distress, either contributing to stigma (Hinshaw, 2005; Zisman-Ilani, Levy-Frank, Hasson-Ohayon, Kravetz, Mashiach-Eizenberg, & Roe, 2013) or by withholding support/preventing access to mental health services (Byrne, 1997; Pescosolido, Perry, Martin, McLeod, & Jensen, 2007), and both are associated with poor mental health outcomes (Kaushik, Kostaki, & Kyriakopoulos, 2016). Concern over future outcomes and loss of adult potential may also constitute a significant

stressor, playing into the self-stigma and fear related to a ‘mental health patient’ or ‘service user’ label (Hinshaw & Stier, 2008).

6.1.2. Psychopathology trajectories in middle childhood

Psychopathology is a complex continuum rather than a single incident, a timeline of antecedents, symptomology, and lasting effects. Thus, it must be discussed as a trajectory over time with implications for future outcomes. In exploring psychopathology in the ALSPAC child cohort, there were 3 main linear trajectories to consider: an increase in difficulties, a decrease, or a relatively stable outcome over the 4 years examined. Within the ‘stable’ trajectory, there was the potential for 2 discreet results: starting with a higher amount of difficulties and remaining constant or starting with a lower amount and remaining so. This pattern of outcomes has been found in multiple cohorts of middle childhood populations examined in context of anxiety (Feng, Shaw, & Silk, 2008), internalising symptomology (Sterba, Prinstein, & Cox, 2007), depression (Whalen, Luby, Tilman, Mike, Barch, & Belden, 2016), ADHD (Barkley, 2016), overall mental health (Forbes, Rapee, Camberis, & McMahon, 2017; Wolpert et al., 2020), and loneliness (Qualter et al., 2013). In addition, this trajectory model in middle childhood has been studied in the relationship of family dysfunction with anxiety (Pagani, Japel, Vaillancourt, Côté, & Tremblay, 2008) the relationship of peer victimisation with psychopathology (Haltigan & Vaillancourt, 2014), and in social withdrawal (Schneider, Younger, Smith, & Freeman, 1998; Oh, Rubin, Bowker, Booth-Laforce, Rose-Krasnor, & Laursen, 2008).

In the abstract, these trajectories are informed by the addition of factors (increased trauma or increased support), the deficit of factors (decreased socialisation or decreased victimisation), or a balance of factors which maintain homeostasis. In practice, this represents the variables that contribute to psychopathology risk and the variables that affect risk. Feng, Shaw, and Silk (2008) focused on personal variables (shyness, insecure attachment, etc.) as a conceptualisation of risk as did Forbes, Rapee, Camberis, and McMahon (2017) with individual traits (reactivity, sociability, etc.). Risk is not an absolute and individual

differences can mediate the relationship between the risk and reality of psychopathology (Bogdan, Hyde, & Hariri, 2013).

Psychopathology trajectories between ages 7 and 11 years were modelled here using the sub-scores and total score from the Strengths and Difficulties Questionnaire (SDQ, Goodman, 1997) which was given to the mother to describe the child's behaviour on 3 occasions during middle childhood. The Hyperactivity sub-scale items measured restless/overactive behaviour, fidgeting, high distractibility and low concentration, impulsivity, and attention span. The Emotional Symptoms sub-scale items measured physical symptomology indicative of anxiety and depression, worrying, sadness/low mood, distress in novel situations, low confidence, and fearful behaviour. The Conduct Problems sub-scale items measured temper and tantrums, fighting with/bullying peers, lying/cheating behaviour, stealing, and general obedience. The Peer Problems sub-scale items measured being solitary/playing alone, being picked on/bullied by others, socialising more with adults than peers, having at least 1 good friend, and being generally liked by peers. The Total Difficulties score is representative of the aggregate sum of the contributory sub-scores.

These sub-scales have been used as predictors/indicators of hyperkinetic and attention-deficit disorders, anxiety, depression, obsessive-compulsive disorders, and conduct and oppositional-defiant disorders, respectively (Achenbach et al., 2008) and are cross-culturally valid (Woerner et al., 2004) though should not be used to compare different cultural populations (de Vries, Davids, Mathews, & Aarø, 2018). In longitudinal studies, the SDQ has been shown to be a valid measure for identifying potential issues and tracking those difficulties over time in a cost-effective manner (Mason, Chmelka, & Thompson, 2012), and results are reliable across samples and age (Keilow, Sievertsen, Niclasen, & Obel, 2019). Becker, Rothenberg, Sohn, and the BELLA Study Group (2014) found that a child population fell into 'normative', 'threshold', and 'atypical' subgroups with baseline scores, resulting a group within mean scoring range, a group with scores approaching the clinical threshold, and a group with scores falling into clinical range. Over 6 years, while most of the population maintained 'normative' status, the small 'atypical' sub-sample remained so, and the 'threshold' sub-sample members

could transition into either group. Stringaris and Goodman (2013) found SDQ scores at baseline were reliable predictors of psychopathology over 3 years. Additionally, the SDQ sub-scores can be utilised in the formation of 'difficulty archetypes', or specific scoring patterns, for use in longitudinal research (Deutz et al., 2018).

In any large representative population containing discreet groups, the sub-population which clusters around the mean, a 'normative' group, will most likely be the largest. When examining such a population with a clinical assessment scale designed to measure non-normative behaviour, it is also assumed that the majority of the study population will be described as normative, with smaller groups varying by degree of the study variable (Vazquez-Leal, Castaneda-Sheissa, Filobello-Nino, Sarimento-Reyes, & Orea, 2012). In a cross-sectional analysis, the individual score or group mean/variance at a single time-point is the focus but longitudinal analysis concentrates on the up/down/static movement of that participant or group, allowing for nuance. A high Hyperactivity score on one day conveys less about the respondent and their experiences than Hyperactivity increasing or decreasing over time. As SDQ scores are reliable predictors of psychopathology along the sub-score domains, a decreasing trajectory would represent improving mental health and an increase representative of worsening psychopathology. Innumerable factors and covariates affect a child's mental health and wellbeing and here the strongest predictors were hypothesised to be the prenatal maternal socialisation profile and degree of child socialisation at age 9.5 years.

Previous studies have found variation in the psychopathologies predicted by the SDQ. Longitudinal twin studies have found the hyperkinetic dimension of ADHD to be stable and have a unipolar relationship with inattentiveness (Greven, Asherson, Rijsdijk, & Plomin, 2011) and while a majority of children above the clinical threshold remain so into young adulthood, there is a sub-sample who see improvement (Sasser, Kalvin, & Bierman, 2016; Lahey, Lee, Sibley, Applegate, Mollina, & Pelham, 2016 as cited in Barkley, 2016). Anxiety and depression are often comorbid (Cohen, Young, Gibb, Hankin, & Abela, 2014) with comorbid trajectories (Snyder, Bullard, Wagener, Leong, Snyder, & Jenkins, 2009; de Lijster et al., 2019) and as above, both vary separately due to a multitude of risk factors (see Albano, Chorpita, & Barlow, 2003; Murray, Creswell, & Cooper, 2009 for

comprehensive reviews on childhood anxiety aetiology and Fleming & Offord, 1990; Heim & Binder, 2012 for depression). Variation has also been explored in conduct and oppositional defiant disorder, with gender affecting trajectory and overlap between the 2 disorders (Maughan, Rowe, Messer, Goodman, & Meltzer, 2004) and trajectory associated with comorbidities (Lavigne, Cicchetti, Gibbons, Binns, Larsen, & Devito, 2001) and later substance abuse (Fergusson, Horwood, & Ridder, 2007). Overall psychopathology trajectories approximating the Total Difficulties score of the SDQ vary in more general terms depending on major risk/predictor variables (Suldo, Thalji, & Ferron, 2010; Christensen, Fahey, Gaillo, & Hancock, 2017; Forbes, Rapee, Camberis, & McMahon, 2017).

The Prosocial sub-scale and sub-score were not utilised directly as part of this model, as it does not factor into the Total Difficulties score, though it was included in the preliminary linear/null model testing. The child social environment was modelled in the previous chapter using a more detailed inventory of self-report data from the child cohort, which better captured the child's perceptions of their own socialisation and value as a social individual. Using the Prosocial sub-score would, which measured prosocial behaviour and not overall socialisation, would be incongruent with the earlier model. The socialisation score derived at age 9.5 years served as a waypoint to examine psychopathology trajectories in this sample before and after the 'snapshot' model of the child social environment.

6.1.3. Latent growth and latent growth mixture modelling

In evaluating cross-sectional data on a population level, some variables, such as weight or height in children, are simple to assess as the majority of the population cluster around the mean, with dwindling proportions in each direction (Hirschhorn et al., 2001). Examining this data as a simple linear association over time is also uncomplicated; as age increases between measurement time points, so will weight or height increase. These analyses and many based on them, assume that the only value in the population is the mean and variance around the mean, with outliers often discounted. Latent class/profile analysis (LCA/LPA) uses cross-sectional observed data to identify latent (unobserved) groups in the population, which differ by group

mean of the studied variable. This strategy was utilised in Chapter 3 to define the maternal cohort by level of socialisation and a similar, longitudinal technique was required in this phase. These conventional analyses are focused on the relationship between the population and the study variable but there is additional value in focusing on the relationship between individuals as associated with the variable (Muthén & Muthén, 2000). The same relationship that defines the latent groups also defines the growth trajectory over time (Muthén, 2004), separating the population by pattern associations into linear models of change.

Latent growth mixture modelling (LGMM; Muthén & Shedden, 1999) is a longitudinal technique used in structural equation modelling to detect latent groups within a population while exploring longitudinal change both within and between those groups (Ram & Grimm, 2009). This technique assumes no set growth parameters and allows for variance by the maximum likelihood of the model being tested (Jung & Wickrama, 2008), with latent trajectories varying around group means rather than the population mean. Whereas intragroup comparison can be accomplished by an ANOVA or regression, the main concern is the mean and interindividual differences are considered error variance (Duncan & Duncan, 2004) and these types of analyses have functional limitations beyond 2 time-points (Andruff, Carraro, Thompson, & Gaudreau, 2009). LGMM is particularly useful in examining developmental trajectories (Bauer & Curran, 2003) as developmental studies are likely to span multiple time-points with repeated measures on a regular interval schedule. Additionally, assuming the standard normal distribution excludes groups of individuals with divergent but non-outlier developmental trajectories (Connell & Frye, 2006), which LGMM can identify.

The past several decades has seen an increased use of LGMM in longitudinal studies, highlighting the effects of variables in one developmental period on future outcomes. Coie, Terry, Lenox, Lochman, and Hyman (1995) used longitudinal growth modelling to explore the effects of childhood rejection and aggression on adolescent psychopathology, finding a gendered association between disorder in adolescence and earlier peer rejection. Koss, George, Davies, Cicchetti, Cummings, and Sturge-Apple (2013) employed an LGMM in determining maladaptive trajectories in child cortisol responses to parental discord. This technique has been

used in identifying latent trajectories in adolescent smoking (Colder et al., 2001) and alcohol use in early adulthood (Colder, Campbell, Ruel, Richardson, & Flay, 2002), covariates predicting specific trajectories in adolescent delinquent behaviour (Wiesner & Windle, 2004), and the effect of low birth weight variance on academic achievement (Espy, Fang, Charak, Minich, & Taylor, 2009). While this method of classification in populations has practical, person-centred applications, it is a probabilistic categorisation and does not represent universal underlying structures (Bauer, 2007).

For any variable being tested in a longitudinal linear model, the only trajectories of change are those of increase, decrease, or stability. Singer and Willett (2003) suggest studies measuring change are beholden to 2 questions: how does change manifest in the measured variable and, what predictions can be made about these changes? This phase of analysis was concerned with change in psychopathology as within the child cohort between ages 7- and 11-years as measured by the SDQ and how psychopathology trajectories differed between latent classes. It was predicted that change would be demonstrated in an 'x configuration' of 4 latent classes: a low-psychopathology group with no change, a high-psychopathology group with no change, a group showing an increase in psychopathology over time, and a group showing a decrease in psychopathology over time. For a robust result, LGMM requires more than 2 time points (Duncan & Duncan, 2004, 2009), and this analysis utilised data at ages 7, 9, and 11 years to track changes in the population through middle childhood.

6.1.4. Study aims

The main aims of this phase of the analysis were to i) use the SDQ to model offspring psychopathology between the ages of 7 and 11 years, ii) determine change over that time, iii) identify discreet groups with divergent psychopathology trajectories and, iv) describe change both within and between those groups over time. Latent growth modelling and mixture modelling were employed as longitudinal forms of structural equation modelling to explore change in psychopathology in this population over 4 years. Psychopathology was approximated using the problem sub-

scores and Total Difficulties score of the SDQ, completed by the maternal cohort at study child ages of 7, 9, and 11 years. It was hypothesised that latent classes existed within the population, differentiated by the experience of psychopathology and that difference would be expressed by an increase/decrease/stable configuration of trajectories as per the literature.

It was originally proposed that the prenatal maternal social environment created a social phenotype which optimised offspring for a specific social environment, existing in a 'mismatch' environment would produce distress, this distress could be measured as the experience of psychopathology, and this was the method by which the prenatal maternal social environment and child social environment influenced offspring mental health outcomes. Creating a longitudinal model set the stage for testing the main thesis in a final analysis before controlling for the effect of the postnatal period. It was further proposed that the difference in psychopathology trajectory between the latent classes, the variance within classes, and class membership was explained by the contribution of the prenatal maternal social environment and child social environment, specifically the maternal prenatal socialisation profile and the child Socialisation at age 9.5 years.

6.2. Methodology

6.2.1. Sample

The main population consisted of ALSPAC Children of the 90s offspring cohort (N=15,645) with cases with missing data excluded (N=9,159). Of the cohort sample, 49.69% were female, 96.09% were white, and 6.22% came from a low-income household (Boyd et al., 2012).

6.2.2. Measures

The Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) was given to the maternal cohort at study child ages 7, 9, and 11 years as part of child-

based surveys. The problem sub-scores and Total Difficulties score were used in this analysis. Full methodology and use details are discussed in Chapter 2 (Section 2.5.4.).

6.2.3. Analytic Strategy

A multi-phase analysis was designed to model offspring psychopathology over time, identify distinct latent groups within this population based on experience of psychopathology, and identify change within and between groups over time. The first step was to determine if change had occurred and then to identify that change by trajectory. While the goal was the best fitting model for the data, preserving parsimony was also important, seeking to explore the complex psychopathological landscape with appropriate paucity.

The initial analysis incorporated latent growth modelling (LGM) to identify change in psychopathology over time. This technique uses longitudinal repeated measure data to plot growth trajectories in a population (Meredith & Tisak, 1990). A linear model was run for each SDQ sub-score and the total difficulties score over 3 time points, which were compared against a null model assuming no change trajectories by holding both the slope and intercept constant at 0. The chi-square (χ^2), Comparative Fit Index (CFI; Bentler, 1990), Tucker-Lewis Index (TLI; Tucker & Lewis, 1973), Root Mean Square Error of Approximation (RMSEA; Steiger, 1990), the Standardised Root Mean Square Residual (SRMR), and the Bayesian information criterion (BIC, Schwarz, 1978) were used to assess goodness-of-fit in linear-null model dyads. The CFI and TLI range between 0 and 1, with a higher result indicating better fit and over .95 being preferable (Hu & Bentler, 1999; Cangur & Ercan, 2015). The RMSEA is a chi-square based measure with a lower result indicating fit (<0.6, Hu & Bentler, 1999) and while a model meeting the cut-offs of CFU/TLI >0.95 and RMSEA <0.6 could be called a best fit model, Xia & Yang (2019) argue additional model justification should be required. The SRMR describes the difference between the observed and expected model, with an absolute value of 0 and a value of <0.08 describing goodness-of-fit (Hu & Bentler, 1999). The BIC is a

criterion informing on fit between different models, with the lower the result, the better the fit.

The next phase of analysis was a latent growth mixture model (LGMM, Muthén & Shedden, 1999) designed to identify latent groups within the population by observed scores and to describe the change over time both within and between groups. The SDQ Total Difficulties score was used as the defining variable at the three time points due to the similar performance off the composite sub-scores with no divergence. A series of linear models estimating a 2-class through 6-class solution were run with no constraints, allowing variance in both the intercept and slope, and run again with the slope variance held constant. Goodness-of-fit was assessed with the BIC, the Lo-Mendel-Rubin likelihood ratio test (LMR-LRT, Lo, Mendel, & Rubin, 2001), and entropy criterion (Celeux & Soromenho, 1996). The BIC is a reliable indicator of model fit, especially when the true model is among the models tested (Vrieze, 2012) but is sensitive to sample size (Wang & Bodner, 2007). The LMR-LRT compares a model with k number of profiles with a model featuring $k - 1$ profiles. In a latent analysis, a non-significant result in the LMR-LRT p-value demonstrates the model with $k - 1$ profiles is a better fit than the proposed model. Entropy represents the amount of uncertainty in any variable's outcomes as a function of its probability (Shannon, 1948), using posterior probabilities to assess the accuracy of an individual's assignment to a class. Values for entropy range from 0 to 1, with a higher entropy value denoting a more accurate classification of the individual into a specific class.

This analysis described change via a linear model with the intercept of each trajectory the mean scores for each latent class at age 7 years and change between time-points represented by the slope. All analyses were performed using Mplus 7 (Muthén & Muthén, 2012)

6.3. Results

This analysis utilised SDQ scores collected from a mother-completed questionnaire at study child ages of 7, 9, and 11 years (Table 6.1). Hyperactivity

scores decreased as a function of age from age 7 (m= 3.00 (IQR= 4.00)) to age 9 (m= 2.00 (IQR= 3.00)) and remained static at age 11 (m= 2.00 (IQR= 3.00)). Emotional Symptoms remained relatively static from age 7 (m= 1.00 (IQR= 2.00)) to age 9 (m= 1.00 (IQR= 2.00)) to age 11 (m= 1.00 (IQR= 2.00)). Conduct Problems remained static over time from age 7 (m= 1.00 (IQR= 2.00)) to age 9 (m= 1.00 (IQR= 2.00)) to age 11 (m= 1.00 (IQR= 2.00)). Peer problems remained static between age 7 (m= 1.00 (IQR= 2.00)) and age 9 (m= 1.00 (IQR= 2.00)) and age 11 (m= 1.00 (IQR= 2.00)). Total Difficulties decreased from age 7 (m= 6.00 (IQR= 6.00)) to age 9 (m= 5.00 (IQR= 6.00)) to age 11 (m= 5.00 (IQR= 5.00)).

Table 6.1. Descriptive statistics for SDQ scores at ages 7, 9, and 11 years

	N	Minimum	Maximum	Median	Interquartile
Age 7 years					
Hyperactivity	8001	0	10	3.00	4.00
Emotional Symptoms	8201	0	10	1.00	2.00
Conduct Problems	8179	0	10	1.00	2.00
Peer Problems	7753	0	10	1.00	2.00
Total Difficulties	7287	0	33	6.00	6.00
Valid	7186				
Age 9 years					
Hyperactivity	7604	0	10	2.00	3.00
Emotional Symptoms	7701	0	10	1.00	2.00
Conduct Problems	7623	0	10	1.00	2.00
Peer Problems	7418	0	10	1.00	2.00
Total Difficulties	6810	0	35	5.00	6.00
Valid	6674				
Age 11 years					
Hyperactivity	6974	0	10	2.00	3.00
Emotional Symptoms	7030	0	10	1.00	2.00
Conduct Problems	6984	0	10	1.00	2.00
Peer Problems	6755	0	9	1.00	2.00
Total Difficulties	6189	0	34	5.00	5.00
Valid	6035				

The sub-scores and the total difficulty score were then examined in a latent growth model (LGM) to determine if there was significant change over time when

compared to a null model. Table 6.2 shows each of the models demonstrate stronger fit than the null model, with higher CFI and TLI, and lower RMSEA, SRMR, and BIC. Parameter estimates for the scores in a linear model are described in Table 6.3, showing the mean intercept, intercept variance, mean slope, slope variance, and intercept-slope correlation for the population sub-scores and total score.

Table 6.2. Fit statistics for the GLM models of the SDQ

Scale	Model	χ^2 (df)	CFI	TLI	RMSEA (90% CI)	SRMR	BIC
Hyperactivity	Null	655.952 (4)	0.893	0.920	0.130 (0.121 - 0.138)	0.077	90275.166
	Linear	**63.80.2 (1)**	**0.990**	**0.969**	**0.080 (0.064 - 0.098)**	**0.016**	**89643.942**
Emotional	Null	62.858 (4)	0.980	0.985	0.039 (0.031 - 0.047)	0.032	83907.198
	Linear	**0.292 (1)**	**1.000**	**1.001**	**0.000 (0.000 - 0.022)**	**0.001**	**83853.654**
Conduct	Null	534.575 (4)	0.848	0.886	0.116 (0.108 - 0.125)	0.087	74357.885
	Linear	**99.818 (1)**	**0.972**	**0.915**	**0.100 (0.084 - 0.117)**	**0.025**	**73775.718**
Peer Problems	Null	110.619 (4)	0.957	0.968	0.052 (0.044 - 0.061)	0.045	73360.878
	Linear	**8.205 (1)**	**0.997**	**0.991**	**0.027 (0.012 - 0.046)**	**0.007**	**73241.251**
Total Difficulties	Null	356.261 (4)	0.917	0.937	0.098 (0.090 - 0.107)	0.073	107400.729
	Linear	**28.579 (1)**	**0.993**	**0.980**	**0.055 (0.039 - 0.073)**	**0.012**	**106968.239**

Table 6.3. Parameter estimates for SDQ scores in a linear model

	Parameter	Coefficient	Standard Error
Hyperactivity	Intercept Mean	3.593	0.032
	Intercept Variance	4.755	0.234
	Slope Mean	-0.291	0.012
	Slope Variance	0.295	0.045
	Intercept - Slope Correlation	-0.532	0.031
Emotional	Intercept Mean	1.540	0.024
	Intercept Variance	2.224	0.182
	Slope Mean	-0.031	0.010
	Slope Variance	0.231	0.037
	Intercept - Slope Correlation	-0.555	0.043
Conduct	Intercept Mean	1.739	0.021
	Intercept Variance	1.719	0.125
	Slope Mean	-0.192	0.008
	Slope Variance	0.149	0.025
	Intercept - Slope Correlation	-0.562	0.039
Peer Problems	Intercept Mean	1.036	0.022
	Intercept Variance	1.566	0.141
	Slope Mean	0.019	0.010
	Slope Variance	0.210	0.030
	Intercept - Slope Correlation	-0.530	0.046
Total Difficulties	Intercept Mean	7.787	0.072
	Intercept Variance	22.976	1.448
	Slope Mean	-0.524	0.028
	Slope Variance	1.649	0.274
	Intercept - Slope Correlation	-0.494	0.041

As the 4 problem sub-scores performed similarly, with no individual sub-score significantly diverging, it was decided to use the Total Difficulties score to model psychopathology across the 3 time points. Models describing a 2-class through 6-class solution were run with slope variance and with slope variance held constant (Table 6.4).

Table 6.4. Fit indices for LGMM with and without slope variance

	BIC	LRT (*p*)	Entropy
With slope variance			
2 classes	103827.170	3118.316 (<0.01)	0.543
3 classes	103504.860	360.029 (0.028)	0.547
4 classes	103197.846	345.062 (<0.01)	0.655
5 classes	102988.355	249.630 (<0.01)	0.604
6 classes	102930.325	101.419 (<0.01)	0.584
Slope variance constant			
2 classes	104686.411	2295.867 (<0.01)	0.504
3 classes	103868.136	831.965 (<0.01)	0.617
4 classes	**103604.014**	**292.594 (<0.01)**	**0.630**
5 classes	103438.228	196.881 (0.050)	0.665
6 classes	103335.341	135.659 (0.033)	0.682

BIC Bayesian information criterion, *LRT* Lo-Mendell-Rubin's adjusted likelihood ratio test

The child cohort population was described in 4 classes (Figure 1) with parameter estimates described in Table 6.5. The Low-Stable class was the largest (N=6,324, 69%), described by a marginal decrease in difficulties over time from an intercept of 4.733 (variance=2.206) with a slope of -0.48. The High-Decreasing class (N=1,490; 16.3%), had the highest rate of difficulties at 7 years but showed a marked decrease by 11 years from an intercept of 12.834 (variance=8.002) with a slope of -3.051. The High-Stable class (N=1,022; 11.2%), showed a marginal increase over the 4 years from an intercept of 11.979 (variance=27.393) with a slope of 0.251. The Low-Increasing class (N=323; 3.5%) was described by a moderate rate of difficulties at 7 years and a sharp increase over time from an intercept of 6.729 (variance=8.030) with a slope of 3.609.

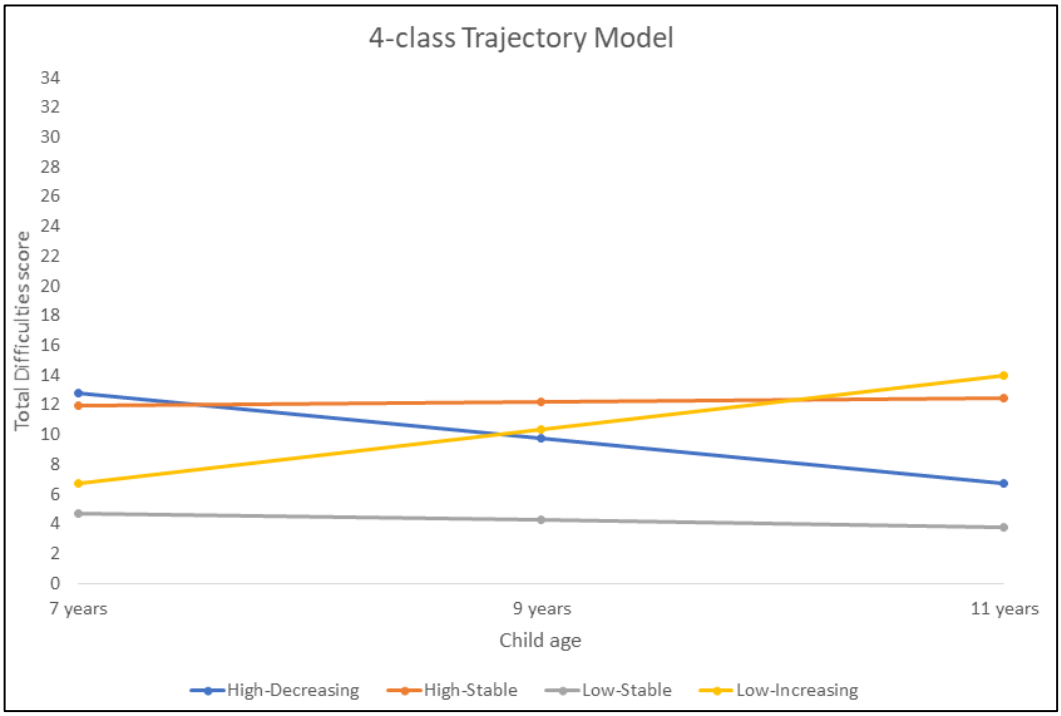

Figure 6.1. 4-class model of psychopathology trajectories from age 7 to 11 years

Table 6.5. Parameter estimates for a 4-class model

	Parameter	Coefficient	Standard Error
Low-Stable	Intercept Mean	4.733	0.069
	Intercept Variance	2.206	0.128
	Slope Mean	-0.480	0.032
	Slope Variance	0.000	0.000
	Intercept - Slope Correlation	0.000	0.000
High-Decreasing	Intercept Mean	12.834	0.286
	Intercept Variance	8.002	0.805
	Slope Mean	-3.051	0.187
	Slope Variance	0.000	0.000
	Intercept - Slope Correlation	0.000	0.000
High-Stable	Intercept Mean	11.979	0.424
	Intercept Variance	27.393	1.882
	Slope Mean	0.251	0.205
	Slope Variance	0.000	0.000
	Intercept - Slope Correlation	0.000	0.000
Low-Increasing	Intercept Mean	6.729	0.390
	Intercept Variance	8.030	1.540
	Slope Mean	3.609	0.341
	Slope Variance	0.000	0.000
	Intercept - Slope Correlation	0.000	0.000

6.4. Discussion

6.4.1. Model Results

In examining the population means for the 4 difficulty sub-scores and the Total Difficulty score of the SDQ, all scores decreased from 7 to 9 years and again from 9 to 11 years. As the population mean could not adequately describe change and variation in psychopathology, a model describing differing trajectories of change was designed. The first analysis assessed if actual statistical change occurred in the population between ages 7 and 11 by using each of the SDQ sub-scores and the Total Difficulties score in an LGM compared against equivalent null models assuming no change. The linear models were the better fit over the null models, indicating change. As none of the difficulty sub-scores significantly diverged in performance over the 3 time-points, the Total Difficulties score was utilised as an aggregate and the defining observed variable in an LGMM to determine class structure within the offspring cohort. It was hypothesised that these groups would be differentiated by the group mean Total Difficulties score at age 7 (intercept) and would follow separate trajectories (linear slope) through ages 9 and 11.

To test the underlying structure, a series of 2-class through 6-class models was run with no parameter constraints, allowing the slope and intercept to vary. When these models were run, each encountered a correlation matrix error for the latent variable with an intercept-slope correlation of 999.00, producing negative variance in the slope. The models were run again with the slope variance held constant and each ran normally. Such errors are not uncommon when running analyses with large populations (Reddon, Jackson, & Schopflocher, 1985) and eliminating the slope variance from the models did not compromise the conceptual integrity of the analyses. Holding the slope variance constant meant assuming the same slope trajectory for each member of each latent class, effectively generalising individual trajectories into group models of change. While sub-populations are not homogeneous groups in lockstep, variance in the intercept here acknowledged the individual differences within each class, even if all members were described by the same generalised trajectory.

After careful exploration, the 4-class model was chosen as the best fit in the series, both in terms of fit indices and contextual value. As predicted by the literature (Oh, Rubin, Bowker, Booth-LaForce, Rose-Krasnor, & Laursen, 2008), the largest class was the 'normative' group, the Low-Stable class. As the defining metric was designed to measure difficulties at thresholds of 'troublesome' behaviour, it was reasonable to expect that a smaller percentage of a representative population would have more extreme difficulties (Vaughn et al., 2011). At 69% of the child cohort population, the members of the Low-Stable class had the lowest rates of difficulties at age 7 (4.733), showing a slight decrease (-0.48) over each time-point. This class had a relatively low intercept variance (2.206), describing a statistically cohesive group in terms of behavioural difficulties at age 7, whose members improved over 4 years in a trajectory which left them doing even better by age 11. As per the mother's evaluations of these children, they seem to have had few difficulties and maintained low levels of psychopathology across middle childhood.

In contrast, the High-Stable class (11.2%) started with a higher rate of difficulties (11.979), which showed a slight increase (0.251) over each time-point in the study period. This class had the highest intercept variance (27.393) in the model, describing a group that varied widely in experience of psychopathology at age 7 but were all identified as stable in those difficulties through age 11. While the scoring guidelines for the parent-rated SDQ lists a Total Difficulties score of 0-13 as normative (sdqinfo.org, 2016), the high variance of the intercept mean indicates this class varied 'up' rather than 'down', as the scale extends to 40 but not below 0. This class remained relatively consistent in problems rather than drastically increasing or decreasing. Not yet exploring the prenatal maternal social environment/child social environment, this stability could be indicative of several influences, including child-onset of an ongoing psychopathology, a confluence of environmental factors, individual differences, or an interaction between them.

As predicted, Low-Increasing and High-Decreasing trajectory classes were present in this model. The High-Decreasing class (16.3%) started with the highest rates of difficulties in the sample (12.834), which steadily declined (-3.051) to moderate rates by age 11. Intercept variance was moderate (8.002), indicating a group with slightly wider range of initial difficulties at age 7, categorised by a sharp

decrease through ages 9 and 11 to a more normative mean. This paints a picture of psychopathology experiences in decline, potentially due to a range of contributory variables, including intervention strategies. The Low-Increasing class (3.5%) started out with the second lowest rates of difficulties (6.729) and steadily increased (3.609) to the highest rates by the end of the study period. This class had a similar intercept variance (8.030), also describing a group with a moderate range of difficulties around a lower mean, categorised by a sharp increase through ages 9 and 11 to end with the highest mean score in the model. That this extreme class is the smallest group in the population is also in keeping with the literature, as the standard distribution of a psychopathologic population will centre on the mean with the most profoundly affected being the fewest (Kessler et al., 2003).

6.4.2. Model discussion

In epidemiological terms, the Low-Stable class might have been described as being of little conceptual value to the thesis hypothesis. It was a large, normative population of SDQ-defined well-adjusted and well-behaved children. However, the value in 'baseline' groups or classes lies in what differentiates them from the rest of the population. The next analysis focused on the prenatal maternal social environment, child social environment, and other potential predictors of class membership for the extreme classes over the baseline. Additionally, the members of the Low-Stable class had only been explored here between the ages of 7 and 11 years, making it very possible that any number of factors changed in their lives, potentially affecting their mental health in adolescence and/or adulthood. Normative groups like the Low-Stable class are not homogeneous, meaning further research could concentrate on latent differences and trajectories within this sub-sample. This group was the largest in the sample, reinforcing that a majority of this population experienced these 4 years of middle childhood without substantial distress. When examined in the context of this project, the Low-Stable class may have represented environmental match; a group of individuals optimised for the environment they lived in, with sufficient advantages and limited disadvantages to affect their mental health and wellbeing.

With its high initial variance, the High-Stable class would also be a promising candidate for in-depth exploration with the expectation of multiple 'stable' classes of varying degrees of severity. In this analysis, it was evident that class members on the lower end of the variance could be considered 'borderline' and those above the class mean were above the clinical threshold (Goodman, Ford, Simmons, Gatward, & Meltzer, 2000; Goodman, Renfrew, & Mullick, 2000). This class comprised 11.2% of this population, approximating prevalence rates of psychopathology in pre-adolescent populations (Roberts, Attkisson, & Rosenblatt, 1998; Meltzer, Gatward, Goodman, & Ford, 2003), though without a definitive mental health diagnosis, this representation of psychopathology was a generalisation. At this stage of the project, it was possible that members of the High-Stable class represented environmental mismatch, chronic social isolation, detrimental environmental and individual factors, and/or an interaction between any of these variables.

The High-Decreasing and Low-Increasing classes showed changed over time in their trajectories, with a future research interest being specific covariate predictors of class membership. What interventions or environmental changes brought about the sharp improvement in the High-Decreasing class and what 'went wrong' in the lives of the Increasing class? It was certainly possible that members of the High-Decreasing class were given appropriate interventions or experienced a radical change, but it was also possible that for some of the membership, their behaviours improved as a result of development throughout middle childhood. The Low-Increasing class may represent a failure of interventions following a distressful change, the onset of a severe childhood psychopathology driven by overwhelming environmental factors (heritability, trauma, etc.), or a confluence of reactive variables. It was hypothesised that Socialisation at 9.5 years may have influenced the trajectories of these 2 classes, that in addition to other contributory factors, the proposed environmental mismatch resulted in distress that was impacted by the prenatal maternal social environment.

6.4.3. Limitations

The results of this analysis cannot be explored without recognising the limitations that were present. As this project utilised secondary data, it was restricted to the variables and schedule in ALSPAC's methodology. More robust results may have come from a longitudinal study specifically designed to model change in psychopathology during middle childhood covalently with change in socialisation, the relationship between the 2, and the impact of the prenatal maternal social environment. Specifically, SDQ measures beginning at age 5 years and running annually through age 12 years, including parent, teacher, and child-rated data, data detailing psychopathology diagnoses and any interventions, and an annual child-completed metric detailing their lived experiences of multiple aspects of socialisation. As with any longitudinal study, attrition was also a concern. While the population for this analysis more than met the criteria assumptions for a valid analysis, cases with missing data were dropped and less attrition would have produced more robust results. In recent years, ALSPAC has moved towards several strategies to address both attrition and incomplete data from participants (Fraser et al., 2013), acknowledging the issue they present.

Psychopathology here is generalised, with distress approximated from the dimensions of the SDQ and not reflective of any clinical diagnoses. Data was also not available on any behavioural, mental health, or medical interventions that may have taken place and which could have contributed to a decline in psychopathology or the maintenance of a stable trajectory. The SDQ was given to the mother who then answered based on her observations of her child's behaviours and not on the child's lived experiences. While the SDQ has robust test-retest reliability (Muris, Meesters, & van de Berg, 2003) and tester-agreement validity (Klasen et al., 2000; Cheng et al., 2018) as used here, it can only approximate the child's experiences. Finally, the representations of distinct latent classes here was a statistical generalisation of child experiences based on the observed SDQ scores and cannot approximate the individual thoughts, feelings, and experiences of cohort members.

6.4.4. Impact and implications

While the use of SDQ data in a longitudinal, latent class examination of difficulties in middle childhood was not a novel analysis, the replication of the 'increase-decrease-stability' model and class percentages reinforces the existent literature. Historically, it was believed that children were not vulnerable to mental illness in the same ways as adults, with symptomology written off as 'bad behaviour' (Lourie & Hernandez, 2003). Those beliefs then centred on a purely medical model of child psychopathology after the rise of psychiatry (Parry-Jones, 1989). Decades of research has led to the contemporary understanding of the roles of genetics/heritability (Blonigen, Hicks, Krueger, Patrick, & Iacono, 2005; Bergen, Gardner, & Kendler, 2007), adverse life events (Pynoos, 1994; Pynoos, Steinberg, & Piacentini, 1999; McLaughlin & Lambert, 2017), and now, epigenetics and second-order effects in childhood and adolescent psychopathology (Goldsmith, Gottesman, & Lemery, 1997; Barker, Walton, & Cecil, 2018). Understanding a child's difficulties as a generalised trajectory over time means understand them, their environment, and their wellbeing in a holistic sense, divorced from the clinical, stigmatising concepts of disorder and mental illness. In short, the implications of this study are the broadening of the literature on psychopathology trajectories in middle childhood but this analysis in context of the overall project speak to a wider understanding of distal influences on child psychopathology.

6.4.5. Conclusions

The modelling of the prenatal maternal social environment and identification of latent socialisation profiles in the maternal cohort established a solid foundation for testing the hypothesis suggesting environmental factors experienced *in utero* could affect offspring mental health outcomes. Modelling the child social environment at age 9.5 years provided a factor of Socialisation by which to measure the child cohort and modelling psychopathology in a longitudinal growth mixture model identified latent trajectories and memberships in those classes. The final step and culmination of these analyses was to determine the effect of the prenatal maternal social environment on psychopathology in middle childhood as determined

by Socialisation, and if that effect was still present after controlling for several covariates during the postnatal period.

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Chapter 7

Testing the impact of socialisation on psychopathology

7.1. Study Introduction

In the previous chapter, change in offspring psychopathology over 4 years of middle childhood was validated and modelled as 4 unique latent trajectory classes. A pattern of a stable low difficulty, stable high difficulty, an increase in difficulties, and a decrease, matched previous longitudinal literature. Having modelled the prenatal maternal social environment, used this model to determine maternal socialisation profiles and predictor covariates during pregnancy, modelled the child social environment with indicator covariates at age 9.5 years as a cross-sectional 'snapshot', and established a pattern of change in psychopathology over 4 years, the remaining steps were to test the hypothesis main effect while also controlling for the influence of the postnatal environment.

The main thesis hypothesised that the prenatal maternal social environment contributed to offspring mental health outcomes via epigenetic processes influenced by the degree of socialisation experienced by the mother while pregnant. The foetal genome would be 'primed' to expect a specific social environment and this social phenotype influenced behaviour and environmental reactions in keeping with the 'expected' environment. This adaptive behaviour would become maladaptive in a differing social environment, creating a mismatch situation which could influence psychopathology risk. Psychopathology risk is also associated with social isolation and it was further hypothesised that offspring of low socialisation mothers would be better equipped for isolation than high socialisation mothers. In the final phase of testing, the maternal socialisation profiles and child socialisation were used in a model exploring: the effect of Socialisation at 9.5 years on membership in a psychopathologic trajectory class during middle childhood, and if that effect was affected by maternal membership in the High or Low Socialisation profile.

Having established an analytical framework to test the main effect hypothesis from the prenatal environment through the cusp of adolescence, it remained to ensure this effect was not due to other contributory variables or environments during the postnatal period of birth through approximately 6 years. These years are a series of critical growth periods and the heightened neuroplasticity of the child's brain means environmental influences could action adaptation enough to contravene the

original epigenetic modifications. A selection of known influences on child and adolescent psychopathology risk were selected as covariates in a control model, including maternal, family environment, and offspring variables. It was hypothesised that the effect of the prenatal maternal social environment would be evident even after controlling for the influences of the postnatal period.

7.1.1. Exploring environmental effects

It is accepted that the prenatal environment is capable actioning physiological effects on both the foetal genome and offspring health outcomes. As the effect of the genome on mental health outcomes is also well established, bringing the two concepts together into the field of behavioural epigenetics seems an obvious next step in the story of psychology. Though backed by decades of replicated research yielding evidence-based results, the main thesis of 'that which affects a pregnant woman can also affect her child' seems simple, almost evocative of old folklore beliefs associating incidental maternal behaviour, such as food cravings, with pregnancy outcomes (Goldfarb, 1988; Schaffir, 2007). Using ALSPAC data to define and then statistically model environments, classify individuals, and determine trajectories made it possible to realistically test this hypothesis. In this chapter, the goal was to bring everything together in a final analysis to explore the main effect of the prenatal maternal social environment on offspring psychopathology.

The prenatal maternal social environment was modelled in the maternal cohort of this population based on a single 13-item inventory describing social support and social networks (Prokhorskas, Ignatyeva, Dragonas, & Golding, 1989), yielding a 5-factor model with the dimensions *Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support*. Individual responses along these dimensions of socialisation explained their social environment during pregnancy and endorsements of these dimensions were used to identify 3 latent social profiles within the maternal cohort population: normative Baseline Socialisation, High Socialisation, and Low Socialisation profiles. To deepen understanding of the characteristics of these profiles, several demographic and individual covariates were regressed onto them to determine which predicted profile membership and when compared against the

Baseline Socialisation profile: membership in the High Socialisation profile was predicted by higher SES and neighbourhood quality, lower interpersonal sensitivity, fewer adverse life events, and the presence of a partner while membership in the Low Socialisation profile was predicted by lower SES and neighbourhood quality, an increased number of adverse life events, and the experiences of discrimination and depression.

The child social environment was modelled in the child cohort of this population based on a single 8-item inventory describing perceptions of social relationships at age 9.5 years (The ALSPAC Study Team, 2009), yielding a unidimensional model of Socialisation. In exploring indicators of Socialisation in this population, a series of demographic and individual covariates were regressed onto this dimension and it was found that maternal childhood home stability and membership in the maternal High Socialisation profile were indicative of higher rates of Socialisation. Change in psychopathology over time in middle childhood was modelled longitudinally using the 4 difficulty sub-scores and Total Difficulties score of the SDQ (Goodman, 1997) given to the maternal cohort in describing their children at ages 7, 9, and 11 years. A latent growth mixture model identified 4 latent trajectory classes of change in psychopathology in this population: Stable Low, Stable High, Increasing, and Decreasing classes.

The penultimate analysis aimed to explore the determinants of psychopathology trajectory class membership in the child cohort by utilising the maternal socialisation profile and child socialisation models. Based on prior literature, it was assumed that child trajectory class would be predicted by maternal profile with child socialisation being a mediating factor. If the ALSPAC data was true to the environmental mismatch theory, the distress of low socialisation at age 9.5 years would be greater for offspring of High Socialisation mothers as offspring of Low Socialisation mothers possessed a protective social phenotype which would impact on isolation distress. It was also possible that offspring of Low Socialisation mothers with higher rates of Socialisation would also express the distress of mismatch, manifested as adaptive psychopathology. The main effect analysis sought to bring together the entire project in a test of the initial hypothesis, followed by a final model to control for the postnatal environment and clarify the strength of the

effect of the prenatal maternal social environment on child psychopathology outcomes in middle childhood.

7.1.2. Controlling for the postnatal environment

The years from birth to approximately age 5-6 are crucial to a child's growth and development, a time of radical physiological, cognitive, emotional, and psychological changes which prepare them for additional development in adolescence and ultimately, adult life. It is a period of increased developmental plasticity (Bateson et al., 2004) as the brain grows rapidly in size, volume, and complexity. Due to this flexibility, the postnatal environment has a profound effect on brain development, which can be either positive and/or negative. An enriched environment with abundant nutrition and normative stress enables healthy development to its fullest potential but a neglectful environment with insufficient nutrition and constant stress brings the risk of deficit and dysfunction. The postnatal environment is more complex than the prenatal maternal social environment, as the child is directly exposed to multiple environments and influencing factors, no longer protected by their mother's body. Poor access to resources such as shelter, nutrition, and medical care have physiological implications, just as abuse, neglect, and trauma contribute to cognitive, emotional, and psychological difficulties. Additionally, several common psychopathologies have moderate to high heritability, meaning an early childhood environment influenced by mental illness in the family and a genome carrying increased risk for that psychopathology.

An unblinking constant in the social sciences is that outcomes are multifactorial in nature. In considering psychopathology, no single factor exists in which exposure results in certain causation. Multiple factors from multiple environments combine with multiple personal and individual factors where the outcome over time is the symptomology and distress of psychopathology. Due to the lack of causal factors, psychopathology is best discussed in terms of predictive variables, risk, and outcomes. This project has viewed the effect of the prenatal maternal social environment on offspring psychopathology not as a causal mechanism, but as a contributor to the variance of these outcomes in a risk model. In

such an analysis, covariates and confounders can be statistically 'held constant' to evaluate the effects of individual variables on the outcome. Thus, this final analysis sought to control for as many major factors from the postnatal environment as possible to examine the contribution of the prenatal maternal social environment on offspring psychopathology to the exclusion of all other factors.

Developmental plasticity is behind the need for this exhaustive attempt at statistically controlling for a complex environment. Brain development during infancy and early childhood could be described as explosive, a flexibility allowing for rapid growth (Bateson et al., 2004; Zelazo & Carlson, 2012) but also for adapting to the immediate environment. Thus, formative experiences that may not be representative of a child's enduring environment can exert an uneven influence, potentially affecting how the child will come to perceive and understand the world. Cognitive schemata, the building blocks of comprehension, develop based on a child's experiences (Georgeon & Ritter, 2011) and remain enduring parts of cognition into adulthood, even if they are incongruent with reality (O'Sullivan & Durso, 1984). This early imprinting is foundational and can be thought of as additional adaptation to the environment, but there is vulnerability in being so experience dependent. Adapting to a negative environment results in maladaptive traits, mechanisms, and coping strategies, and this dysfunctional development increases the risk of psychopathology in childhood, adolescence, and adulthood. Fischer, Ayoub, Singh, Noam, Maraganore, and Raya (1997) suggest these adaptations constitute specific environmental-dependent developmental pathways to psychopathology. This additional risk from maternal and environmental factors had to be held constant when considering the effect of the prenatal maternal social environment of psychopathology outcomes.

7.1.2.1 The Postnatal Environment: Maternal Influence

The quote, "*Mother is the name for God in the lips and hearts of little children*," (Thackeray, 1848/2003; vol. 2, pp. 26) eloquently sums up maternal influence during the postnatal period. An infant relies completely upon her for survival and even as dependence decreases while independence increases, she

remains a powerful influence in most aspects of the child's life. The idea of 'nature versus nurture' originated in philosophical debate over the true nature of man but by the latter half of the 20th century, centred on genetic predeterminism versus lived experience. Many critics of behavioural genetics felt such positions refuted parental influence on a child and the issue became highly polarised during the 1980s and 1990s (Begley, 1998). It is now quite well established that both the individual genome and the family environment are major contributors in who the child is and who they will become (Gibson, 2008; Burga & Lehner, 2012). 'Nurture' as a shorthand for the parental labour of raising a child does a disservice to the depth of emotional investment and actual influence on all pursuant outcomes in the child's life. Both the intentional acts of parenting and the unintentional aspects of the family environment affect risk of poor physical and mental health outcomes, with the mother being a central figure in this environment.

A mother's life and experiences while raising her children, and how those experiences affect them, can be most easily described in terms of benefits and deficits. Enjoying psychological wellbeing, high socialisation, abundant emotional support, positive parenting experiences, and few adverse life events would convey considerable benefits (Eisenberg et al., 2001). Conversely, the experiences of maternal childhood trauma, mental illness, unpleasant parenting experiences, socioeconomic disparity, and the burden of major life events would constitute significant deficits for both the mother and children. Benefits reduce or impact the risk of psychopathology while deficits increase that risk. Variables describing maternal psychopathology, social/emotional support, general attitudes on parenting, and life events were sourced for analysis in this model for both their positive and negative effects on offspring.

It is well accepted that maternal mental illness has a profound effect on the entire family (Hinshaw, 2005; Reupert & Maybery, 2007) but children are particularly vulnerable from birth through middle childhood (Oyserman, Mowbray, Meares, & Firminger, 2000). Psychopathology variables used in this analysis included the anxiety, somatic symptoms, and depression sub-scores of the Crown-Crisp Experimental Index (CCEI; Crown & Crisp, 1966, 1970). While these were considered sperate variables, it was important to note the prevalence of comorbidity

among ‘common’ mental illnesses and the interactions between these and other psychosocial covariates.

Over the past several decades, research into postnatal depression, its presentation and symptomology, and effects has shone light on this ‘hidden’ problem. As with other mental illnesses, presentation of postnatal depression varies (Beck & Indman, 2005; Bågedah-Strindlund & Börjesson, 2007), with many unable to identify their experiences as depression (Bilszta, Ericksen, Buist, & Milgrom, 2010) and others unwilling to disclose those experiences (Hall, 2006; Dennis, 2009). The debate continues over whether postnatal depression is clinically distinct from major depressive disorder, with the timing of the episode being the defining difference in the DSM-5 (American Psychiatric Association, 2013). Batt, Duffy, Novick, Metcalf, and Epperson (2020) lay out several similarities and differences between the 2 disorders along epigenetic, psychosocial, neural, hormonal, and genetic dimensions, suggesting that even if postnatal depression is distinct from all other depressive disorders, there is benefit in treating it as if it were the same. Postnatal depression has a significant impact on a mother’s identity. A meta-data-analysis of qualitative studies identified the theme of “*failing to live up to*” the ideal of motherhood and being unable to express this feeling, perpetuating a cycle of self-doubt and fear of negative evaluation leading to isolation (Knudson-Martin & Silverstein, 2009).

Postnatal depression is also detrimental to the new baby and other children in the household. A major theme of postnatal depression has been described as the delta between the anticipated experience of motherhood and the actual experience (Beck, 2002), lowering parental enjoyment and impairing the mother-child relationship (Murray, Cooper, Wilson, & Romaniuk, 2003; Moehler, Brunner, Wiebel, Reck, & Resch, 2006). Depressed mothers may be less reactive to the child’s needs (Paulson, Dauber, & Leiferman, 2006; Field, 2010) which affects trust and attachment style (McMahon, Barnett, Kowalenko, & Tennant, 2006). Maternal postnatal depression is associated with lower rates of cognitive and emotional development (Cogill, Caplan, Alexandra, Robson, & Kumar, 1986; Beck, 1989; Murray, Hipwell, Hooper, Stein, & Cooper, 1996) as well as behavioural problems during early childhood (Philipps & O’Hara, 1991; Grace, Evindar, & Stewart, 2003), adjustment problems in school

(Sinclair & Murray, 1998), and increased risk of poor mental health outcomes (Murray, Arteche, Fearon, Halligan, Goodyer, & Cooper, 2011).

While there is evidence that postnatal maternal anxiety is associated with internalising symptomology in children (Barker, Jaffee, Uher, & Maughan, 2011), there is also evidence associating anxiety with child somatic symptomology and psychopathology (Glasheen, Richardson, & Fabio, 2009). Qiu et al. (2013) found that in a developmental comparison, prenatal maternal anxiety influenced right hippocampal size and postnatal anxiety limited growth of the left hippocampus, and there is evidence of maternal anxiety adversely affecting child temperament (Henrichs et al., 2009; Blair, Glynn, Sandman, & Davis, 2011). Young children are very perceptive and could instinctively perceive maternal anxiety as an indicator of danger or threat, meaning an activation of their own stress response. Consistent activation of the HPA axis during the stress response is associated with increased psychopathology risk, particularly anxiety disorders (Faravelli et al., 2012).

General attitudes on parenting were represented by variables including maternal enjoyment and confidence. While it is a common occurrence for new mothers to worry they're doing 'everything wrong', chronic low maternal confidence and enjoyment are associated with depressive symptomology (Reck, Noe, Gerstenlauer, & Stehle, 2012) while higher confidence mediates parenting stress (Liu, Chen, Yeh, & Hsieh, 2012). Lack of maternal bonding can be indicative of psychopathology (O'Higgins, Roberts, Glover, & Taylor, 2013) and is evident in poor maternal-foetal bonding during pregnancy (Dubber, Reck, Müller, & Gawlik, 2015; Rossen et al., 2016). The effects of early parenting attitudes on the child are far-reaching, particularly poor maternal bonding, which has been associated with depression (Hall, Peden, Rayens, & Beebe, 2004; Kraaij et al., 2003) and psychopathy in adulthood (Gao, Raine, Chan, Venables, & Mednick, 2009), as well as cognitive and developmental problems (Johnson, 2013). Child perceptions of poor parental bonding were also found to be associated with depression in a clinical sample (Key, 1995). Low maternal enjoyment and confidence can influence bonding and produce behaviour which can affect the child's attachment style (Pederson, Moran, Sitko, Campbell, Ghesquire, & Acton, 1990; Moss, Rousseau, Parent, St-

Laurent, & Saintonge, 1998), resulting in maladaptive schemata (Mason, Platts, & Tyson, 2005).

Adverse life event variables used in this analysis included absence of a partner, the relationship of the mother's parents, domestic violence by and/or against the mother, and an inventory of major/adverse life events. The presence/absence of a partner was used as a proxy for support stress, describing a potential amount of emotional and practical support which was either present or lacking. The presence of a partner was a significant predictor of memberships in the High Socialisation profile during pregnancy and the absence of a partner is a well-accepted stressor when balancing life with raising a child alone (Weinraub & Wolf, 1983; Cairney, Boyle, Offord, & Racine, 2003). Maternal parental relationship was included due to its effect on the child's adult relationships (Yu & Adler-Baeder, 2007) and adult attachment style (Levy, Blatt, & Shaver, 1998).

Domestic violence constitutes trauma for the victim, both in the context of a single occurrence or an ongoing pattern of abuse (Jones, Hughes, & Unterstaller, 2001). It is also traumatic for children in the family (McCloskey & Walker, 2000), either witnessing their mother being abused or her abusing someone else. Specifically, the trauma of domestic violence is principally associated with poor adjustment (Levendosky & Graham-Bermann, 2001), behavioural problems (Fantuzzo & Mohr, 1999; Moylan, Herrenkohl, Sousa, Tajima, Herrenkohl, & Russo, 2010), difficulties with emotional and social functioning (Kolbo, Blakely, & Engelman, 1996; Fantuzzo & Mohr, 1999), and psychopathology (Davies, Winter, & Cicchetti, 2006; Graham-Bermann, Gruber, Howell, & Girz, 2009) among other issues. The adverse life events inventory was included, as that which was traumatic for the mother likely affected the child and the family environment. To return to the quote at the beginning of this section, during infancy and early childhood, a mother is the centre of her child's life and it has been well demonstrated that maternal trauma has an effect on children's psychosocial and emotional development (Muller-Nix, Forcada-Guex, Pierrehumbert, Jaunin, Borghini, & Ansermet, 2004; van Ee, Kleber, & Mooren, 2012; Briggs et al., 2014).

7.1.2.2. The Postnatal Environment: Child Experiences

A child's experiences from infancy through early childhood not only guide their development, but also define how they perceive the world and interact with it throughout the rest of their life. Lived experiences become models for adaptive 'operating procedures' for use in similar situations, even if those procedures are faulty. A toddler who is rewarded with nutritious snacks may develop healthy eating patterns in adolescence and adulthood, but a toddler who walks on eggshells when an abusive parent is drunk may develop maladaptive methods of relating to others. This project has discussed a remarkable number of environments, experiences, and other factors which can adversely affect a child in a staggering number of ways and of these, trauma is significant. Thus, the child-based variables used in this phase of analysis were adverse and major life events over several time-points in infancy and early childhood. As in Chapter 4, these were represented by the traumatic experiences of being taken into care, physical abuse, and sexual abuse.

Over the past several decades, adverse childhood experiences (ACEs) have been recognised as one of the leading contributory factors to psychopathology both in childhood/adolescence (Flaherty et al., 2013) and adulthood (Schilling, Aseltine, & Gore, 2007; Reuben et al., 2016), as well as being significant predictors poor physical health outcomes (Felitti et al., 1998; Brown et al., 2009) and substance abuse vulnerability (Dube et al., 2003; 2006). Childhood trauma is also the largest causal factor in the development of PTSD during childhood/adolescence (World Health Organization, 1992). Not every adverse event is perceived as trauma by the child, will result in PTSD, or will lead to the child developing a mental or physical illness. As with most influencing variables, ACEs must be discussed in terms of risk and a substantial body of literature has found that ACEs significantly increase the risk negative health and mental health outcomes. Due to the predictive association of these events with later psychopathology, they were included in the control model.

7.1.2.3. Mother/Child Socialisation Categorisation

Each individual was predicted to follow a specific psychopathology trajectory based on the maternal socialisation profile as a reaction to their own socialisation. A 9-category variable was created for the child cohort, sorting individuals into matrix cells based on their mother's prenatal maternal social environment profile and their child social environment tertile. 'Mismatch' categories described those with social environments that differed from their predicted environments: maternal high/child low (MHCL), maternal medium/child low (MMCL), maternal low/child medium (MLCM), maternal high/child medium (MHCM), maternal low/child high (MLCH), and maternal medium/child high (MMCH). 'Matching' categories described those with social environments with the same conditions for mother and child: maternal low/child low (MLCL), maternal medium/child medium (MMCM), and maternal high/child high (MHCH). It was predicted that the 'mismatch' category individuals would experience higher levels of distress as explained by psychopathology trajectory while 'matching' category individuals would experience less distress.

While not the specific focus of this research, environmental match was important within the offspring cohort. The Stable-Low psychopathology trajectory was assumed to be populated by children who existed in an environment matching that which they were primed to experience. With low levels of distress persisting across middle childhood, they were assumed to be enjoying the benefits of environmental match or the multiple environmental effect that produced their mental wellbeing. It also should be noted that the maternal High Socialisation profile was 53.5% of the population and the normative Baseline profile accounted for a further 36.5%, leaving only a small percentage of the overall population (10%) with low socialisation. Adequate to high socialisation appears to have been the norm in this population, which can then be generalised to the greater UK population (Golding et al., 2001), meaning that environmental match was common at this time in the UK.

These predictions focused on the high/low dynamic based on the existing literature surrounding both socialisation and environmental mismatch. Those with moderate socialisation, the normative Baseline Socialisation mothers and 2nd tertile

Socialisation children, were not predicted to follow any specific trajectory based solely on their mother/child socialisation category. Based on the literature, it was assumed that the offspring of Baseline mothers did not undergo any epigenetic modifications to insulate them from a harsh environment or acclimate them to a highly socialised environment. The outcome for these individuals was predicted as a psychopathology trajectory dependent solely on the child's socialisation, with low socialisation resulting in distress and high/medium socialisation showing a lack of distress. For children in the 2nd tertile for Socialisation born to Low or High Socialisation mothers, no significant distress was predicted as the moderate levels of socialisation would be 'close enough' to the expected environment and not constitute true environmental mismatch.

7.1.3. Study Aims

This phase of the project featured 2 analyses with unique goals. In exploring the main effect of the thesis, this chapter sought to i) determine the effect of membership in the maternal High/Low Socialisation profiles on offspring membership in the psychopathological trajectory classes in middle childhood and, ii) if this effect was affected by offspring Socialisation at 9.5 years. Sourcing maternal and child variables from the postnatal period allowed for i) establishing a model to statistically control for the effects of potentially confounding covariates and, ii) determining if the main effect results were present when controlling for the postnatal period. It was hypothesised that the prenatal maternal social environment, as represented by the maternal socialisation profiles, would be predictive of offspring mental health outcomes in middle childhood, represented by psychopathology trajectory class. It was further hypothesised that this effect would be affected by Socialisation at 9.5 years and be present after controlling for the postnatal period.

A 2-stage multinomial logistic regression was performed to identify prenatal and postnatal maternal covariates and early childhood covariates with influence on psychopathology trajectory. Once identified, these covariates were statistically controlled for in a second model to determine which mother/child socialisation categories were likely to follow which psychopathology trajectories in middle

childhood. This final set of analyses would determine the existence of a main effect of the prenatal maternal social environment on offspring child psychopathology once the effects of the postnatal/family environment were controlled for.

7.2. Methodology

7.2.1. Sample

The main population consisted of ALSPAC Children of the 90s offspring cohort (N=15,645). Of the cohort sample, 49.69% were female, 96.09% were white, and 6.22% came from a low-income household (Boyd et al., 2012).

Data from the maternal ALSPAC cohort was also utilised (N=15,645). Mean age for this population was 27.77 years (SD=4.91 years) with a range of 15-45. Most respondents had lived in the Avon catchment area for at least a year: 53.4% had lived in/near Avon all their lives, 16.9% over 10 years, 11.2% between 5 and 9 years, 13.6% between 1 and 4 years, and 5% for under a year (Herrick, Golding, and the ALSPAC Study Team, 2008). The population was further described as 79.1% homeowners, 79.4% married, and 97.8% were white/Caucasian (Fraser et al., 2013).

Cases with missing data were dropped from both cohorts, resulting in a combined population of N=2913.

7.2.2. Measures

7.2.2.1. Thesis derived measures

For this analysis, 3 of the measures used were derived variables from previous phases of the project, socialisation profile membership for the maternal cohort, rate of socialisation in the child cohort, and trajectory of psychopathology over middle childhood. These derived variables are discussed in Chapter 2 (Section 2.5.5.1.).

7.2.2.2. Maternal covariates

Several demographic and previously utilised prenatal variables were included in this analysis: the mother's age at delivery, socioeconomic status (SES), neighbourhood quality, the presence of a partner, maternal childhood home distruption, and maternal childhood sexual abuse (see Chapter 2, Section 2.5.1.). In controlling for the influence of the postnatal period, multiple maternal variables were chosen concerning postnatal psychopathology (postnatal anxiety, somatic symptoms, and depression), general attitudes on parenting (maternal enjoyment and maternal confidence), and life events from the child's birth to age 6 years. Details and methodologies of these measures and covariates are discussed in Chapter 2 (Section 2.5.5.2.).

7.2.2.3. Child-based covariates

Child gender and adverse life events from age 1.5 to 8.5 years were included in this analysis, as discussed in Chapter 2 (Section 2.5.3.1.).

7.2.3. Analytic strategy

A 2-stage multinomial logistic regression was designed to first determine which covariates had independent effects on psychopathology trajectory in middle childhood. This type of analysis was favoured over a moderation interaction analysis as the objective was to determine the type of interaction by level of variable. The trajectories were regressed onto the selected covariates described above using the prenatal maternal socialisation latent class profiles and child socialisation tertiles as predictors. The Low-Stable trajectory, prenatal maternal High Socialisation profile, and child socialisation 3rd tertile (high) were used as reference categories. Covariates with no effect were not included in the second model. The second model used the 9-category 'mismatch' variable as the primary predictor variable, controlling for the selected covariates, to determine which psychopathology trajectories had the highest

likelihood of membership based on mother/child socialisation category. The Low-Stable trajectory and mother-high/child-high (MHCH) category were used as reference categories. Both models were run in SPSS Ver. 25 (IBM Corp., 2017).

While results are expressed in terms of likelihood or an odds ratio, the use of multinomial logistic regression assumes case dependency for variables, that each individual case has a definite value for each variable. To fit the assumptions of this technique, probabilistic variables were quantified as definite. Multinomial logistic regression was used for its ability to accommodate both categorical and continuous variables in a model examining categorical outcomes.

7.3. Results

Population counts in the maternal cohort (N=12,548) prenatal socialisation profiles are described in Table 7.1, with the High Socialisation profile the largest at 53.42%, the Baseline Socialisation profile at 36.47%, and the Low Socialisation profile the smallest at 10.11%.

Table 7.1. Population counts and percentages of maternal prenatal socialisation profiles

	Population	Valid Percentage
High Socialisation	6,703	53.42
Baseline Socialisation	4,576	36.47
Low Socialisation	1,269	10.11
Valid	12,548	100.00
Missing	3,097	
TOTAL	15,645	

Population counts of the child cohort (N=4,181) in socialisation are described in Table 7.2 as tertiles of Low, Medium, and High.

Table 7.2. Population counts and percentages of child socialisation tertiles

	Population	Valid Percentage
Low	1,393	33.3
Medium	1,394	33.3
High	1,394	33.3
Valid	4,181	100.00
Missing	11,464	
TOTAL	15,645	

Population counts in the child cohort (N=9,159) middle childhood psychopathology trajectories are described in Table 7.3, with the Stable Low trajectory the largest at 69.04%, Decreasing trajectory at 16.27%, the Stable High trajectory at 11.16%, and the Increasing difficulties trajectory the smallest at 3.53% of the population.

Table 7.3. Population counts and percentages of child psychopathology trajectories

	Population	Valid Percentage
Stable Low difficulties	6,324	69.04
Decreasing difficulties	1,490	16.27
Stable High difficulties	1,022	11.16
Increasing difficulties	323	3.53
Valid	9,159	100.00
Missing	6,486	
TOTAL	15,645	

The valid child cohort population was assigned a socialisation category based on the maternal socialisation profile and the child socialisation tertile, resulting in 9 categories described below in Table 7.4 with abbreviated here as M_C_. The categories with mothers from the High Socialisation profile were the largest (18.7% for MHCH, 18.3% for MHCM, and 16% for MHCL), followed by those with mothers from the Baseline Socialisation profile (12.9% for MMCL, 11.7% for MMCM, and 11.4% for MMCH), with categories including mothers from the Low

Socialisation profile being the smallest (4.4% for MLCL, 3.4% for MLCM, and 3.3% for MLCH).

Table 7.4. Population counts and percentages of maternal/child socialisation categories

	Population	Valid Percentage
Maternal Low, Child Low	184	4.4
Maternal Medium, Child Low	538	12.9
Maternal High, Child Low	671	16.0
Maternal Low, Child Medium	141	3.4
Maternal Medium, Child Medium	488	11.7
Maternal High, Child Medium	765	18.3
Maternal Low, Child High	136	3.3
Maternal Medium, Child High	475	11.4
Maternal High, Child High	783	18.7
Valid	4,181	100.0
Missing	11,464	
TOTAL	15,645	

Table 7.5 below describes the maternal cohort by the demographic and prenatal covariates used in this analysis. Maternal age at delivery (N=14,069) ranged from 15-44 years (M=28 (SD=4.96)) and neighbourhood quality (N=13,041) ranged from 0-12 (M=8.08 (SD=2.27)). Maternal parental relationship scores retrospectively asked at 33 months (N=8,664), ranged from 0-21 (M=14.87 (SD=4.18)). Maternal SES by simplified NS-SEC showed that intermediate occupations comprised the highest percentage of the cohort (32.2%), followed by lower managerial/administrative/professional occupations (24.2%), semi-routine occupations (21.3%), routine occupations (13.5%), higher managerial/administrative/professional occupations (5.9%), lower supervisory/technical occupations (2.6%), and the small employers/own account workers were the smallest percentage of the cohort at 0.4%. The population counts detailing the presence of a partner in the maternal cohort are also displayed with full 92.3% of the valid population having a partner while 7.7% did not.

Table 7.5. Maternal demographics and prenatal covariates descriptive statistics and population counts

	N	Minimum	Maximum	Mean	Std. Deviation
Maternal age	14,069	15	44	28	4.96
N. Quality	13,041	0	12	8.08	2.27
Parental relationship	8,664	0	21	14.87	4.18

	Population	Valid Percent.
Simplified NS-SEC		
Higher managerial/administrative/professional	657	5.9
Lower managerial/administrative/professional	2,696	24.2
Intermediate	3,579	32.2
Small employers/own account workers	40	0.4
Lower supervisory/technical	286	2.6
Semi-routine	2,367	21.3
Routine	1,496	13.5
Valid	11,121	100.0
Missing	4,524	
TOTAL	15,645	
Presence of a partner		
Yes	7,348	92.3
No	612	7.7
Valid	7,960	100.0
Missing	7,686	
TOTAL	15,645	
Childhood home disruption		
No	8,766	72.7
Yes	3,289	27.3
Valid	12,055	100.0
Missing	3,590	
TOTAL	15,645	
Childhood sexual abuse		
Did not occur	7,937	70.7
Stranger	1,758	15.7
Non-stranger	1,533	13.6
Valid	11,228	100.0
Missing	4417	
TOTAL	15,645	

Descriptive statistics for the maternal Crown-Crisp Experimental Index (CCEI) sub-scores for Anxiety, Somatic Symptoms, and Depression over 4 time-points are described in Table 7.6. Anxiety and Depression had ranges of 0-16 and Somatic Symptoms had a range of 0-14 for each time-point. Mean Anxiety scores increased steadily from 8 weeks (M=3.42 (SD=3.328)), to 8 months (M= 3.61 (SD=3.355)), to 21 months (M=3.78 (SD=3.346)), to 33 months (M=4.71 (SD=3.580)). Mean Somatic Symptom scores fluctuated but remained relatively stable from 8 weeks (M=2.61 (SD=1.816)), to 8 months (M=2.57 (SD=1.900)), to 21 months (M=2.68 (SD=1.963)), to 33 months (M=2.87 (SD=2.080)). Mean Depression scores declined steadily from 8 weeks (M=3.53 (SD=3.048)), to 8 months (M=3.35 (SD=3.014)), to 21 months (M=2.95 (SD=2.713)) before a sharp increase at 33 months (M=4.21 (SD=3.218)). Table 7.7 shows the population counts of anxiety, somatic symptoms, and depression occurrence after recording for an upper 45% clinical threshold and summarising each domain by clinical instance at any time point over the postnatal period.

Table 7.6. Descriptive statistics for Crown-Crisp Experiential Index sub-scores

	N	Minimum	Maximum	Mean	Std. Deviation
8 weeks					
Anxiety	11,809	0	16	3.42	3.328
Somatic	11,809	0	14	2.61	1.816
Depression	11,805	0	16	3.53	3.048
8 months					
Anxiety	11,319	0	16	3.61	3.355
Somatic	11,321	0	14	2.57	1.900
Depression	11,320	0	16	3.35	3.014
21 months					
Anxiety	10,386	0	16	3.78	3.346
Somatic	10,384	0	14	2.68	1.963
Depression	10,385	0	16	2.95	2.713
33 months					
Anxiety	9,561	0	16	4.71	3.580
Somatic	9,600	0	14	2.87	2.080
Depression	9,533	0	16	4.21	3.218
Valid	8,302				
Missing	7,343				
TOTAL	15,645				

Table 7.7. Population counts of clinical instances of anxiety, somatic symptoms, and depression during the postnatal period

	Population	Valid Percentage
Anxiety		
No	6,500	77.0
Yes	1,939	23.0
Valid	8,439	100.0
Missing	7,207	
TOTAL	15,645	
Somatic Symptoms		
No	7,822	92.4
Yes	642	7.6
Valid	8,464	100.0
Missing	7,182	
TOTAL	15,645	
Depression		
No	6,972	82.9
Yes	1,435	17.1
Valid	8,407	100.0
Missing	7,239	
TOTAL	15,645	

Descriptive statistics for maternal attitude scores are presented in Table 7.8. Mean Maternal Enjoyment ranged from 0-15 at 8 weeks, 1-15 at 33 months, and 5-30 when combined. This score decreased slightly between 8 weeks (M=13.21 (SD=2.140)) and 33 months (M=13.05 (SD=2.256)) with a combined sample mean for this period of M=26.26(SD=3.82)). Mean Maternal Confidence ranged from 2-18 at both time points and 7-36 when combined. This score also decreased between 8 weeks (M=15.04 (SD=2.070)) and 33 months (M=14.52 (SD=2.220)) with a combined sample mean for this period of M=29.54(SD=3.66)).

Table 7.8. Descriptive statistics for maternal attitude scores at 2 time points and overall

	N	Minimum	Maximum	Mean	Std. Deviation
8 weeks					
Maternal Enjoyment	11,114	0	15	13.21	2.14
Maternal Confidence	11,182	2	18	15.04	2.07
33 months					
Maternal Enjoyment	9,557	1	15	13.05	2.25
Maternal Confidence	9,558	2	18	14.52	2.22
Combined					
Maternal Enjoyment	8,972	5	30	26.26	3.82
Maternal Confidence	9,023	7	36	29.54	3.66
Valid	8,846				
Missing	6,799				
TOTAL	15,645				

Frequencies describing the experience of domestic violence are listed in Table 7.9. In exploring domestic violence by the mother against the partner, 99.4% had not done so and 0.6% had. Regarding domestic violence against the mother by the partner, 99% had not been so victimised and 1% had. After recoding for overall instance, domestic violence had not occurred in 98.7% of the valid study households and was present in 1.3%.

Table 7.9. Population counts and percentages of domestic violence

	Population	Valid Percentage
Mother has beaten partner		
No	7,231	99.4
Yes	41	0.6
Valid	7,272	100.0
Missing	8373	
TOTAL	15,645	
Partner has beaten mother		
No	7,196	99.0
Yes	77	1.0
Valid	7,273	100.0
Missing	8,372	
TOTAL	15,645	
Combined domestic violence		
No	7,171	98.7
Yes	96	1.3
Valid	7,267	100.0
Missing	8,379	
TOTAL	15,645	

Maternal adverse life events are described in Table 7.10. Mean number of events ranged from 0-34 at 8 months (M=3.54 (SD=2.524)) and increased sharply at 8 months (M=5.24 (SD=4.020)), ranging from 0-40. These experiences decreased at 21 months (M=4.48 (SD=2.929)), ranging from 0-23, but increased by 33 months (M=5.10 (SD=3.170)), ranging from 0-24.

Table 7.10. Descriptive statistics for maternal adverse life events over 4 time-points

	N	Minimum	Maximum	Mean	Std. Deviation
8 weeks	11,810	0	34	3.54	2.524
8 months	11,314	0	40	5.24	4.020
21 months	10,388	0	23	4.48	2.929
33 months	9,717	0	24	5.10	3.170

Population counts of gender in the child cohort are shown below in Table 7.11. In this sub-population, males were slightly more populous (51.2%) than females (48.8%).

Table 7.11. Population counts and percentages of child gender

	Population	Valid Percentage
Male	7,699	51.2
Female	7,349	48.8
Valid	15,048	100.0
Missing	597	
TOTAL	15,645	

Frequencies and percentages of adverse events in the child cohort are described in Table 7.12. Rates of these experiences (defined as being taken into care, abuse, or sexual abuse) remained relatively static between ages 1.5 years and 8.5 years, varying between 97.4% and 96% experiencing no adverse life events and between 2.6% and 4% having had one or more of these experiences.

Table 7.12. Population counts and percentages of child adverse events over 7 time-points

	Frequency	Valid Percentage
1.5 Years		
No	10,765	97.4
Yes	284	2.6
Missing	4,596	
TOTAL	15,645	100.0
2.5 Years		
No	9,833	96.0
Yes	406	4.0
Missing	5,406	
TOTAL	15,645	100.0
3.5 Years		
No	9,717	96.7
Yes	328	3.3
Missing	5,600	
TOTAL	15,645	100.0
5 Years		
No	9,067	96.0
Yes	376	4.0
Missing	6,202	
TOTAL	15,645	100.0
6 Years		
No	8,330	96.5
Yes	301	3.5
Missing	7,014	
TOTAL	15,645	100.0
7 Years		
No	8,176	96.8
Yes	266	3.2
Missing	7,203	
TOTAL	15,645	100.0
8.5 Years		
No	7,855	96.0
Yes	330	4.0
Missing	7,460	
TOTAL	15,645	100.0

A multinomial logistical regression was run with all chosen covariates to determine which affected either the prenatal maternal social environment or child social environment. Psychopathology trajectories in middle child were used as the outcome variable with maternal socialisation profile and child socialisation tertiles as predictors. The stable-low trajectory was used as a reference category. Significant predictors of the high-decreasing trajectory (Table 7.13) were childhood sexual abuse of the mother by a stranger (OR = 1.487, 95% CI = 1.042, 2.122), postnatal somatic symptoms (OR = 2.093, 95% CI = 1.212, 3.614), maternal enjoyment (OR = 0.942, 95% CI = 0.906, 0.980) and confidence (OR = 0.923, 95% CI = 0.882, 0.965), adverse life events at 8 weeks (OR = 1.093, 95% CI = 1.022, 1.169), child gender (OR = 0.669, 95% CI = 0.515, 0.869), trauma at age 2.5 years (OR = 1.985, 95% CI = 1.026, 3.841), 7 years (OR = 2.236, 95% CI = 1.121, 4.460), 8.5 years (OR = 2.116, 95% CI = 1.083, 4.133), and scoring within the 1st tertile for socialisation at 9.5 years (OR = 2.087, 95% CI = 1.518, 2.869). Significant predictors of the high-stable trajectory (Table 7.14) were maternal age at delivery (OR = 0.960, 95% CI = 0.925, 0.996), SES (OR = 1.092, 95% CI = 1.004, 1.188), neighbourhood quality (OR = 0.926, 95% CI = 0.869, 0.987), postnatal somatic symptoms (OR = 1.951, 95% CI = 1.083, 3.514), maternal enjoyment (OR = 0.954, 95% CI = 0.912, 0.998) and confidence (OR = 0.925, 95% CI = 0.879, 0.973), child gender (OR = 0.591, 95% CI = 0.437, 0.798), trauma at age 7 years (OR = 4.154, 95% CI = 2.070, 8.337), 8.5 years (OR = 2.287, 95% CI = 1.111, 4.706), and scoring within the 1st tertile for socialisation at 9.5 years (OR = 2.059, 95% CI = 1.436, 2.953). The only significant predictors of the low-increasing trajectory (Table 7.15) were trauma at age 5 years (OR = 2.476, 95% CI = 1.022, 6.002) and scoring within the 1st tertile for socialisation at 9.5 years (OR = 2.088, 95% CI = 1.267, 3.441).

Table 7.13. Multinomial logistic regression of maternal and child covariates on the high-decreasing psychopathology trajectory

	Unadj.	Std. Error	Chi-square	df	Sig.	OR	95% CI
Maternal age	-0.021	0.016	1.584	1	0.208	0.980	0.949 – 1.012
SES	0.057	0.038	2.212	1	0.137	1.058	0.982 – 1.141
Neighbour. quality	-0.004	0.029	0.017	1	0.898	0.996	0.941 – 1.055
Partner	17.609	2772.906	0.000	1	0.995	†	0.000 – 0.000
Maternal parents	0.012	0.017	0.449	1	0.503	1.102	0.978 – 1.047
Home disruption	-0.765	0.600	1.627	1	0.202	0.456	0.144 – 1.508
Abuse (stranger)	**0.397**	**0.181**	**4.789**	**1**	**0.029***	**1.487**	**1.042 – 2.122**
Abuse (non-stranger)	0.183	0.193	0.899	1	0.343	1.201	0.822 – 1.754
Postnatal anxiety	0.361	0.190	3.592	1	0.580	1.434	0.988 – 2.083
Postnatal somatic	**0.739**	**0.279**	**7.022**	**1**	**0.008****	**2.093**	**1.212 – 3.614**
Postnatal depression	-0.119	0.217	0.302	1	0.583	0.888	0.581 – 1.358
Mat. enjoyment	**-0.060**	**0.020**	**8.985**	**1**	**0.003****	**0.942**	**0.906 – 0.980**
Mat. confidence	**-0.080**	**0.023**	**12.239**	**1**	**0.000*****	**0.923**	**0.882 – 0.965**
Domestic violence	0.391	0.631	0.384	1	0.536	1.479	0.429 – 5.098
Life events 8 wks.	**0.089**	**0.034**	**6.772**	**1**	**0.009****	**1.093**	**1.022 – 1.169**
Life events 8 mos.	0.004	0.020	0.030	1	0.862	1.004	0.964 – 1.044
Life events 21 mos.	0.002	0.030	0.005	1	0.942	1.002	0.945 – 1.063
Life events 33 mos.	0.034	0.027	1.606	1	0.205	1.035	0.981 – 1.091
Child gender	**-0.402**	**0.133**	**9.062**	**1**	**0.003****	**0.669**	**0.515 – 0.869**
Trauma 1.5 years	-0.774	0.471	2.701	1	0.100	0.461	0.183 – 1.161
Trauma 2.5 years	**0.686**	**0.337**	**4.150**	**1**	**0.042***	**1.985**	**1.026 – 3.841**
Trauma 3.5 years	0.315	0.392	0.646	1	0.421	1.370	0.636 – 2.955
Trauma 5 years	0.434	0.334	1.690	1	0.194	1.544	0.802 – 2.971
Trauma 6 years	-0.476	0.383	1.549	1	0.213	0.621	0.293 – 1.315
Trauma 7 years	**0.805**	**0.352**	**5.221**	**1**	**0.022***	**2.236**	**1.121 – 4.460**
Trauma 8.5 years	**0.749**	**0.342**	**4.811**	**1**	**0.028***	**2.116**	**1.083 – 4.133**
Child soc. 1st tertile	**0.736**	**0.162**	**20.529**	**1**	**0.000*****	**2.087**	**1.518 – 2.869**
Child soc. 2nd tertile	0.031	0.175	0.032	1	0.858	1.032	0.732 – 1.454
Child soc. 3rd tertile	.	.	.	.	.	.	.
Maternal social low	0.364	0.222	2.675	1	0.102	1.438	0.930 – 2.224
Maternal social med.	0.155	0.146	1.121	1	0.290	1.167	0.877 – 1.554
Maternal social high	.	.	.	.	.	.	.

*p<0.05; **p<0.01; ***p<0.001; † stack overflow in Hessian matrix; child socialisation 3rd tertile and maternal socialisation high are reference categories

Table 7.14. Multinomial logistic regression of maternal and child covariates on the high-stable psychopathology trajectory

	Unadj.	Std. Error	Chi-square	df	Sig.	OR	95% CI
Maternal age	**-0.041**	**0.019**	**4.837**	**1**	**0.028***	**0.960**	**0.925 – 0.996**
SES	**0.088**	**0.043**	**4.242**	**1**	**0.039***	**1.092**	**1.004 – 1.188**
Neighbour. quality	**-0.077**	**0.032**	**5.645**	**1**	**0.018***	**0.926**	**0.869 – 0.987**
Partner	0.386	8330.978	0.000	1	1.000	1.471	0.000 – 0.000
Maternal parents	-0.004	0.019	0.044	1	0.833	0.996	0.959 – 1.034
Home disruption	-0.704	0.679	1.073	1	0.300	0.495	0.131 – 1.874
Abuse (stranger)	0.182	0.212	0.736	1	0.391	1.200	0.792 – 1.818
Abuse (non-stranger)	-0.209	0.234	0.796	1	0.372	0.811	0.513 – 1.284
Postnatal anxiety	0.357	0.212	2.823	1	0.093	1.429	0.942 – 2.167
Postnatal somatic	**0.668**	**0.300**	**4.950**	**1**	**0.026***	**1.951**	**1.083 – 3.514**
Postnatal depression	0.312	0.231	1.830	1	0.176	1.366	0.869 – 2.146
Mat. enjoyment	**-0.047**	**0.023**	**4.272**	**1**	**0.039***	**0.954**	**0.912 – 0.998**
Mat. confidence	**-0.078**	**0.026**	**8.975**	**1**	**0.003****	**0.925**	**0.879 – 0.973**
Domestic violence	0.238	0.710	0.113	1	0.737	1.269	0.316 – 5.103
Life events 8 wks.	0.029	0.039	0.544	1	0.461	1.029	0.953 – 1.112
Life events 8 mos.	0.012	0.023	0.248	1	0.619	1.012	0.967 – 1.058
Life events 21 mos.	0.051	0.034	2.308	1	0.129	1.052	0.985 – 1.124
Life events 33 mos.	0.024	0.030	0.622	1	0.430	1.024	0.965 – 1.087
Child gender	**-0.526**	**0.153**	**11.758**	**1**	**0.001****	**0.591**	**0.437 – 0.798**
Trauma 1.5 years	-0.430	0.523	0.677	1	0.410	0.650	0.234 – 1.811
Trauma 2.5 years	0.151	0.429	0.124	1	0.724	1.163	0502 – 2.696
Trauma 3.5 years	0.503	0.435	1.334	1	0.248	1.653	0.704 – 3.880
Trauma 5 years	-0.573	0.484	1.401	1	0.237	0.564	0.219 – 1.456
Trauma 6 years	-0.609	0.432	1.990	1	0.158	0.544	0.233 – 1.268
Trauma 7 years	**1.424**	**0.355**	**16.050**	**1**	**0.000*****	**4.154**	**2.070 – 8.337**
Trauma 8.5 years	**0.827**	**0.368**	**5.045**	**1**	**0.025***	**2.287**	**1.111 – 4.706**
Child soc. 1st tertile	**0.722**	**0.184**	**15.436**	**1**	**0.000*****	**2.059**	**1.436 – 2.953**
Child soc. 2nd tertile	-0.069	0.203	0.116	1	0.733	0.933	0.627 – 1.389
Child soc. 3rd tertile	.	.	.	.	.	.	.
Maternal social low	0.083	0.262	0.100	1	0.752	1.086	0.650 – 1.815
Maternal social med.	0.275	0.165	2.780	1	0.095	1.317	0.953 – 1.820
Maternal social high	.	.	.	.	.	.	.

*p<0.05; **p<0.01; ***p<0.001; child socialisation 3rd tertile and maternal socialisation high are reference categories

Table 7.15. Multinomial logistic regression of maternal and child covariates on the low-increasing psychopathology trajectory

	Unadj.	Std. Error	Chi-square	df	Sig.	OR	95% CI
Maternal age	-0.029	0.026	1.206	1	0.260	0.971	0.922 – 1.023
SES	-0.123	0.068	3.251	1	0.071	0.884	0.774 – 1.011
Neighbour. quality	0.046	0.048	0.925	1	0.336	1.047	0.954 – 1.149
Partner	0.310	0.000	0.000	1	†	1.364	1.364 – 1.364
Maternal parents	-0.010	0.027	0.142	1	0.706	0.990	0.939 – 1.044
Home disruption	10.754	245.829	0.002	1	0.965	†	†
Abuse (stranger)	0.052	0.314	0.028	1	0.868	1.054	0.569 – 1.950
Abuse (n-stranger)	0.321	0.287	1.247	1	0.264	1.378	0.785 – 2.419
Postnatal anxiety	0.311	0.308	1.015	1	0.314	1.364	0.745 – 2.498
Postnatal somatic	0.355	0.439	0.655	1	0.418	1.426	0.604 – 3.368
Postnatal depress.	0.624	0.327	3.645	1	0.056	1.867	0.984 – 3.544
Mat. enjoyment	0.010	0.034	0.095	1	0.758	1.010	0.946 – 1.080
Mat. confidence	-0.035	0.037	0.861	1	0.353	0.966	0.898 – 1.039
Domestic violence	0.831	0.802	1.072	1	0.300	2.296	0.476 – 11.064
Life events 8 wks.	0.015	0.056	0.074	1	0.785	1.015	0.910 – 1.132
Life events 8 mos.	-0.013	0.033	0.158	1	0.691	0.987	0.926 – 1.052
Life events 21 mos.	0.089	0.046	3.821	1	0.051	1.093	1.000 – 1.195
Life events 33 mos.	0.007	0.043	0.027	1	0.870	1.007	0.926 – 1.095
Child gender	0.080	0.212	0.144	1	0.705	1.084	0.715 – 1.642
Trauma 1.5 years	-0.898	0.797	1.269	1	0.260	0.407	0.085 – 1.944
Trauma 2.5 years	0.200	0.546	0.133	1	0.715	1.221	0.418 – 3.563
Trauma 3.5 years	0.786	0.527	2.225	1	0.136	2.196	0.781 – 6.170
Trauma 5 years	**0.907**	**0.452**	**4.028**	**1**	**0.045***	**2.476**	**1.022 – 6.002**
Trauma 6 years	-0.685	0.668	1.050	1	0.305	0.504	0.136 – 1.869
Trauma 7 years	0.515	0.551	0.874	1	0.350	1.674	0.568 – 4.933
Trauma 8.5 years	0.630	0.523	1.454	1	0.228	1.878	0.674 – 5.234
Child soc. 1st tertile	**0.736**	**0.255**	**8.351**	**1**	**0.004****	**2.088**	**1.267 – 3.441**
Child soc. 2nd tertile	0.035	0.282	0.015	1	0.901	1.036	0.596 – 1.801
Child soc. 3rd tertile	.	.	.	.	.	.	.
Maternal social low	0.263	0.369	0.508	1	0.476	1.301	0.631 – 2.683
Maternal social med.	0.104	0.231	0.201	1	0.654	1.109	0.705 – 1.744
Maternal social high	.	.	.	.	.	.	.

*$p<0.05$; † stack overflow in Hessian matrix; child socialisation 3rd tertile and maternal socialisation high are reference categories

Non-significant covariates did not need to be controlled for and were dropped from the model. A second multinomial logistic regression was run with the psychopathology trajectories as the outcome variable and the maternal/child socialisation categories as the main predictor variable. The low-stable trajectory and the MHCH category were the reference categories. In examining socialisation by 'mismatch' categories, the MLCL (OR = 2.442, 95% CI = 1.343, 4.439), MMCL (OR = 2.303, 95% CI = 1.492, 3.555), MHCL (OR = 2.208, 95% CI = 1.473, 3.308), and MMCM (OR = 1.840, 1.185, 2.859) category offspring were likely to follow the high-decreasing trajectory (Table 7.16, Table 7.19). Further, the MMCL (OR = 3.072, 95% CI = 1.891, 4.990) and MHCL (OR = 2.089, 95% CI = 1.285, 3.396) category offspring were likely to follow the high-stable trajectory (Table 7.17, Table 7.19). Finally, the MMCL (OR = 2.422, 95% CI = 1.265, 4.639) and the MLCH (OR = 2.782, 95% CI = 1.063, 7.277) category offspring were likely to follow the low-increasing trajectory (Table 7.18, Table 7.19).

Table 7.16. Multinomial logistic regression of predictor control covariates and socialisation categories on the high-decreasing psychopathology trajectory

	Unadj.	Std. Error	Chi-square	df	Sig.	OR	95% CI
Maternal age	**-0.030**	**0.014**	**4.503**	**1**	**0.034***	**0.971**	**0.945 – 0.998**
SES	**0.067**	**0.032**	**4.253**	**1**	**0.039***	**1.069**	**1.003 – 1.139**
Neighbour. quality	-0.018	0.025	0.528	1	0.467	0.982	0.935 – 1.031
Abuse (stranger)	0.244	0.157	2.432	1	0.119	1.276	0.939 – 1.735
Postnatal somatic	**0.744**	**0.220**	**11.446**	**1**	**0.001****	**2.105**	**1.368 – 3.239**
Mat. enjoyment	**-0.051**	**0.017**	**8.776**	**1**	**0.003****	**0.950**	**0.919 – 0.983**
Mat. confidence	**-0.089**	**0.019**	**20.783**	**1**	**0.000*****	**0.915**	**0.881 – 0.951**
Life events 8 wks.	**0.096**	**0.026**	**14.054**	**1**	**0.000*****	**1.101**	**1.047 – 1.158**
Child gender	**-0.297**	**0.116**	**6.615**	**1**	**0.010***	**0.743**	**0.592 – 0.932**
Trauma 1.5 years	-0.290	0.389	0.557	1	0.456	0.748	0.349 – 1.604
Trauma 2.5 years	0.451	0.276	2.675	1	0.102	1.569	0.914 – 2.693
Trauma 5 years	0.475	0.288	2.725	1	0.099	1.608	0.915 – 2.827
Trauma 7 years	**0.798**	**0.299**	**7.100**	**1**	**0.008****	**2.221**	**1.235 – 3.994**
Trauma 8.5 years	**0.703**	**0.293**	**5.737**	**1**	**0.017***	**2.019**	**1.136 – 3.587**
MLCL	**0.893**	**0.305**	**8.567**	**1**	**0.003****	**2.442**	**1.343 – 4.439**
MMCL	**0.834**	**0.221**	**14.194**	**1**	**0.000*****	**2.303**	**1.492 – 3.555**
MHCL	**0.792**	**0.206**	**14.738**	**1**	**0.000*****	**2.208**	**1.473 – 3.308**
MLCM	0.351	0.365	0.924	1	0.336	1.421	0.694 – 2.907
MMCM	**0.610**	**0.225**	**7.368**	**1**	**0.007****	**1.840**	**1.185 – 2.859**
MHCM	0.172	0.216	0.637	1	0.425	1.188	0.778 – 1.812
MLCH	0.646	0.344	3.525	1	0.060	1.907	0.972 – 3.742
MMCH	0.288	0.240	1.435	1	0.231	1.334	0.833 – 2.137
MHCH	.	.	.	.	.	.	.

*p<0.05; **p<0.01; ***p<0.001; MHCH is reference category

Table 7.17. Multinomial logistic regression of predictor control covariates and socialisation categories on the high-stable psychopathology trajectory

	Unadj.	Std. Error	Chi-square	df	Sig.	OR	95% CI
Maternal age	**-0.062**	**0.016**	**14.986**	**1**	**0.000*****	**0.939**	**0.910 – 0.970**
SES	0.065	0.037	3.080	1	0.079	1.067	0.992 – 1.148
Neighbour. quality	**-0.082**	**0.028**	**8.712**	**1**	**0.003****	**0.921**	**0.872 – 0.973**
Abuse (stranger)	0.274	0.178	2.367	1	0.124	1.315	0.928 – 1.863
Postnatal somatic	**0.818**	**0.239**	**11.748**	**1**	**0.001****	**2.267**	**1.420 – 3.620**
Mat. enjoyment	**-0.052**	**0.020**	**7.001**	**1**	**0.008****	**1.082**	**0.914 – 0.987**
Mat. confidence	**-0.100**	**0.022**	**20.322**	**1**	**0.000*****	**0.905**	**0.866 – 0.945**
Life events 8 wks.	**0.078**	**0.030**	**7.056**	**1**	**0.008****	**1.082**	**1.021 – 1.146**
Child gender	**-0.402**	**0.134**	**9.075**	**1**	**0.003****	**0.669**	**0.515 – 0.869**
Trauma 1.5 years	-0.315	0.452	0.488	1	0.485	0.729	0.301 – 1.768
Trauma 2.5 years	0.262	0.325	0.648	1	0.421	1.299	0.687 – 2.459
Trauma 5 years	-0.419	0.407	1.060	1	0.303	0.658	0.296 – 1.461
Trauma 7 years	**1.203**	**0.309**	**15.106**	**1**	**0.000*****	**3.329**	**1.815 – 6.106**
Trauma 8.5 years	**1.070**	**0.300**	**12.714**	**1**	**0.000*****	**2.916**	**1.619 – 5.250**
MLCL	0.655	0.349	3.526	1	0.060	1.926	0.972 – 3.817
MMCL	**1.122**	**0.247**	**20.561**	**1**	**0.000*****	**3.072**	**1.891 – 4.990**
MHCL	**0.737**	**0.248**	**8.828**	**1**	**0.003****	**2.089**	**1.285 – 3.396**
MLCM	0.535	0.395	1.832	1	0.176	1.707	0.787 – 3.705
MMCM	0.400	0.273	2.141	1	0.143	1.492	0.873 – 2.549
MHCM	0.056	0.262	0.046	1	0.830	1.058	0.633 – 1.769
MLCH	0.438	0.410	1.140	1	0.286	1.549	0.694 – 3.461
MMCH	0.448	0.272	2.705	1	0.100	1.565	0.918 – 2.670
MHCH	.	.	.	.	.	.	.

*p<0.05; **p<0.01; ***p<0.001; MHCH is reference category

Table 7.18. Multinomial logistic regression of predictor control covariates and socialisation categories on the low-increasing psychopathology trajectory

	Unadj.	Std. Error	Chi-square	df	Sig.	OR	95% CI
Maternal age	**-0.058**	**0.024**	**5.932**	**1**	**0.015***	**0.944**	**0.901 – 0.989**
SES	**-0.123**	**0.061**	**4.126**	**1**	**0.042***	**0.884**	**0.785 – 0.996**
Neighbour. quality	0.010	0.042	0.053	1	0.817	1.010	0.929 – 1.097
Abuse (stranger)	-0.076	0.282	0.073	1	0.787	0.927	0.533 – 1.611
Postnatal somatic	0.500	0.382	1.715	1	0.190	1.648	0.780 – 3.482
Mat. enjoyment	-0.003	0.030	0.012	1	0.913	0.997	0.940 – 1.057
Mat. confidence	**-0.076**	**0.033**	**5.408**	**1**	**0.020***	**0.927**	**0.870 – 0.988**
Life events 8 wks.	0.064	0.044	2.161	1	0.142	1.066	0.979 – 1.162
Child gender	0.242	0.192	1.591	1	0.207	1.274	0.874 – 1.857
Trauma 1.5 years	-0.802	0.773	1.075	1	0.300	0.449	0.099 – 2.042
Trauma 2.5 years	0.264	0.466	0.321	1	0.571	1.302	0.522 – 3.246
Trauma 5 years	0.826	0.424	3.785	1	0.052	2.283	0.994 – 5.246
Trauma 7 years	0.342	0.518	0.437	1	0.509	1.408	0.510 – 3.883
Trauma 8.5 years	**0.997**	**0.434**	**5.282**	**1**	**0.022***	**2.710**	**1.158 – 6.341**
MLCL	0.704	0.511	1.899	1	0.168	2.022	0.743 – 5.503
MMCL	**0.885**	**0.332**	**7.118**	**1**	**0.008****	**2.422**	**1.265 – 4.639**
MHCL	0.600	0.319	3.541	1	0.060	1.823	0.975 – 3.406
MLCM	-0.142	0.772	0.034	1	0.855	0.868	0.191 – 3.941
MMCM	0.009	0.398	0.000	1	0.982	1.009	0.462 – 2.201
MHCM	0.000	0.339	0.000	1	0.999	1.000	0.515 – 1.942
MLCH	**1.023**	**0.491**	**4.347**	**1**	**0.037***	**2.782**	**1.063 – 7.277**
MMCH	-0.081	0.409	0.039	1	0.843	0.922	0.413 – 2.057
MHCH	.	.	.	.	.	.	.

*p<0.05; **p<0.01; MHCH is reference category

Table 7.19. Psychopathology trajectories by mother/child socialisation category

	High-Decreasing	High-Stable	Low-Increasing	Low-Stable
MLCL	2.442	†	†	.
MMCL	2.303	3.072	2.422	.
MHCL	2.208	2.089	†	.
MLCM	†	†	†	.
MMCM	1.840	†	†	.
MHCM	†	†	†	.
MLCH	†	†	2.782	.
MMCH	†	†	†	.
MHCH	.	.	.	.

† nonsignificant likelihood; Low-Stable, MHCH are reference categories

7.4. Discussion

7.4.1. Model Results

A multinomial logistic regression model was designed and loaded with a bank of maternal and child covariates with potential influence on development during the post-natal period, with the prenatal maternal socialisation profiles and the child socialisation tertiles used as factors. These covariates were regressed onto the middle childhood psychopathology trajectories to determine which were predictive of membership, and the Low-Stable trajectory, maternal high socialisation profile, and child socialisation 3rd tertile (high socialisation) were used as reference categories. The design of this model was intended to identify covariates which affected trajectory for inclusion in a final model. The second step was to design a model incorporating only the significant predictor covariates in order to control for their influence on psychopathology trajectory in middle childhood. The 9-category variable of mother/child socialisation categories was used as the factor in a multinomial logistic regression with psychopathology trajectory as the dependent variable. The reference categories were the Low-Stable trajectory and maternal-high/child-high (MHCH) category.

The maternal-low/child-low category (MLCL; OR=2.442, 95% CI = 1.343, 4.439) showed the highest likelihood of following the High-Decreasing trajectory, with the maternal-medium/child-low (MMCL; OR=2.303, 95% CI = 1.492, 3.555) second, followed by the maternal-high/child-low category (MHCL; OR=2.208, 95% CI = 1.473, 3.308), and finally, the maternal-medium/child-medium category (MMCM; OR=1.840, 95% CI = 1.185, 2.859). Assuming no interventions and controlling for influential covariates, all children with low socialisation at 9.5 years were likely to experience an alleviation of distress, regardless of maternal prenatal socialisation profile. This was also true for children with moderate socialisation born to normative socialisation mothers, though the likelihood was not as great. Members of the MMCL (OR = 3.072, 95% CI = 1.891, 4.990) and MHCL (OR = 2.089, 95% CI = 1.285, 3.396) were also highly likely to follow the High-Stable trajectory. The

data describes a consistent level of high psychopathology in middle childhood for the children of mothers with normative socialisation during pregnancy who were in low socialisation environments at age 9.5 years, and for the children of high socialisation mothers who were also in low-socialisation environments. Children 'primed' *in utero* for normative or high social environments suffered distress in low social environments. Children from the MMCL category (OR=2.422, 95% CI = 1.265, 4.639) and the maternal-low/child-high category (MLCH; OR=2.782, 95% CI = 1.063, 7.277) were highly likely to follow the Low-Stable trajectory. Children prenatally 'primed' for social isolation experienced increased distress when in a highly social environment, effectively in environmental mismatch.

7.4.2. Model discussion

In total, the offspring born to mothers with membership in the maternal Low Socialisation profile reacted to socialisation levels in middle childhood either with decreasing distress (low socialisation children) or increasing distress (high socialisation children). The MLCM category was not significantly likely to follow any of the examined trajectories, indicating either a potential prevalence for the Low-Stable reference trajectory or no statistical likelihood for any trajectory as a group. Moderate levels of socialisation appeared to trigger no appreciable distress or maladaptive social behaviours. The children of mothers in the normative Baseline Socialisation profile had a more complex trajectory profile, as those with low levels of socialisation were likely to follow all 3 trajectories but had the highest likelihood of the High-Stable trajectory, those with moderate levels following the High-Decreasing (with the lowest odds ratio of the sample), and those with high levels again either following the reference Low-Stable trajectory or lacking a solid group likelihood. Children of High Socialisation profile mothers with low socialisation were likely to follow High-Decreasing or High-Stable trajectories, with those enjoying moderate socialisation non-significant for any trajectory as above, and those with high socialisation being a reference category.

Maternal childhood sexual abuse by a stranger was the only prenatal covariate to show an effect on the post-natal period, reflecting the far-reaching

effects of abuse on adult psychopathology (Beitchman, Zucker, Hood, DaCosta, Akman, & Cassavia, 1992; Jumper, 1995), especially interpersonal relationships (Mullen, Martin, Anderson, Romans, & Herbison, 1994), and has been associated with change in parenting behaviours and mother/child relationships in the ALSPAC cohort (Roberts, O'Connor, Dunn, Golding, & the ALSPAC Study Team, 2004). Postnatal somatic symptoms had the largest effect on this trajectory and are indicative of postnatal psychopathology (Williamson, O'Hara, Stuart, Hart, & Watson, 2014), as well as being associated with child hyperactivity in both early childhood and adolescence in the ALSPAC cohort (Bolea-Alamañac et al., 2019). Lower maternal enjoyment and confidence during the first 3 years of motherhood predicted higher distress in middle childhood. Lower levels of both constructs are predictive of postnatal psychopathology (Mori, Tsuchiya, Maehara, Iwata, Sakajo, & Tamakoshi, 2017) and can affect child attachment style (Zimmer-Gembeck, Webb, Thomas, & Klag, 2015) and mother-child relationships (Roberts, O'Connor, Dunn, Golding, & the ALSPAC Study Team, 2004). Caring for a new-born constitutes a significant stressor (Harriman, 1983) and the addition of an adverse life event when the infant is only 8 weeks old has the potential to be quite affecting, as it was a significant predictor here.

Model results for the High-Decreasing trajectory showed multiple significant predictor covariates and described mothers who experienced child sexual abuse and postnatal distress while feeling unfulfilled/unconfident in parenting and dealing with adverse events early in the postnatal period. Their children were likely to have been male, experienced trauma in early and/or middle childhood, had low levels of socialisation in middle childhood, and experienced high levels of distress at age 7 years which decreased sharply by age 11. Model results for the High-Stable trajectory yielded fewer significant covariates and described younger mothers with lower SES living in poorer quality neighbourhoods and who also suffered postnatal distress, lower maternal enjoyment, and lower maternal confidence. Their children were likely to have been male, experienced trauma, and low socialisation during middle childhood in addition to consistent high levels of psychopathology between ages 7 and 11 years. For the Low-Increasing trajectory, only 2 covariates were significant predictors, and this model described a population with the only defining

features being a child taken into care, experiencing physical, and/or sexual abuse at the end of early childhood alongside low socialisation in middle childhood.

As trauma was defined here as being taken into care, physical and/or sexual abuse, it described a pattern of instability rather than a single traumatic event such as a car accident or accidental injury. Experiencing one of these events at age 2.5 years during a crucial development period here predicted initially high but decreasing levels of psychopathology. Trauma at ages 7 and 8.5 years may have accounted for the high rates of distress at the beginning of the study period but may have been addressed with behavioural or medical intervention, reducing distress and psychopathology symptomology. Trauma in early childhood has been shown to have lasting psychosocial (Briggs-Gowan, Carter, Clark, Augustyn, McCarthy, & Ford, 2010; Lieberman, Chu, Van Horn, & Harris, 2011) and neurodevelopmental effects (Pynoos, Steinberg, & Piacentini, 1999), including impacting social functioning (Cole & Putnam, 1992; Perry & Pollard, 1998). It is possible that the prevalence of early trauma in sub-samples contributed to social isolation at age 9.5 years, which in turn contributed to increasing distress across middle childhood.

Lower maternal age is associated with postnatal psychopathology risk (Webster, Thompson, Mitchell, & Werry, 1994; Deal & Holt, 1998), impaired psychosocial skills in offspring (Fergusson & Woodward, 1999), and specifically with conduct disorder in male children (Wakschlag, Gordon, Lahey, Leober, Green, & Leventhal, 2000). Younger mothers are also less likely to possess higher educational qualifications and more likely to have experienced adverse life events and isolation during pregnancy and the postnatal period (Black, Fleming, & Rome, 2012), in addition to the postnatal somatic symptoms and lower maternal enjoyment and confidence described in this sub-sample. Socioeconomic factors have been discussed several times throughout this thesis but the relationship between lower SES, lower neighbourhood quality, and poor individual outcomes maintained its relevancy throughout. The combined ‘weight’ of these covariates potentially produced a family environment that compounded these risks and in concert with trauma in middle childhood and social isolation, resulted children with a consistently high experience of distress. This group may have been resistant to intervention or, due to socioeconomic factors, did not receive adequate intervention.

The results here validate the main effect hypotheses: i) low socialisation mothers with low socialisation offspring had decreasing psychopathology, potentially the result of protective prenatal adaptations, ii) high socialisation mothers with low socialisation offspring had high levels of psychopathology in a 'mismatch' social environment and, iii) low socialisation mothers with high socialisation offspring showed increasing psychopathology in a 'mismatch' social environment. Moderate child socialisation was a non-issue with the exception of the MMCM category, who followed the High-Decreasing trajectory, and moderate maternal prenatal socialisation was a secondary in impact to child level of socialisation. These findings indicate that the potential for behavioural epigenetic adaptation and resultant maladaptive mismatch may only be present in extreme social environments.

It is important to note that low prenatal maternal socialisation was not a significant independent predictor of psychopathology trajectory in the first control model, meaning that any effect in the second stage model was the result of the interaction between the prenatal maternal social environment and the child social environment. There was no direct effect of prenatal maternal social isolation on offspring psychopathology without impact by child social environment. This result confirms the possibility of epigenetic priming for a specific social environment with maladaptive outcomes in the event of environmental mismatch. A harsh/deficit social environment on its own was not enough to significantly increase the risk of high or increasing psychopathology in middle childhood, rather it provided a measure of resilience from the distress of isolation but produced distress in highly socialised offspring. In examining the effect sizes of trajectory likelihood, the 'mismatch' categories delivered strong effects as all were >2. In particular, the MMCL category had an odds ratio of 3.072 (95% CI = 1.891, 4.990) for the High-Stable trajectory and the MLCH category showed a high effect size for the Low-Increasing trajectory (2.782 (95% CI = 1.063, 7.277). These results are encouraging because of their strength after controlling for postnatal variables, indicating a definite effect.

The findings from this control model are also important as they highlight the many socio-demographic and psychosocial variables that had an effect on child

psychopathology outcomes. While the models presented in this analysis expressly sought to control for their impact, it was because they carried such an impact that control was necessary. The effect of the prenatal maternal social environment x child social environment interaction was identified as significant independent of these covariates, but the lives of the maternal and child cohorts occurred outside of a theoretical model. Trauma still wounded, psychopathology was still suffered, and low socialisation still isolated these individuals, regardless of the statistical significance of their lived experiences.

7.4.3. Limitations

While the results of this final analysis are encouraging in their implications, they must be viewed in light of several limitations. The first and most important of these is the amount of attrition in the valid sample size due to missing data. Compliance in a longitudinal study is always at its height in the beginning, with increasing attrition as time passes (Twisk & de Vente, 2002; Young, Powers, & Bell, 2006) and while this has been discussed in previous chapters, the impact was greatest for this phase of the analysis. Additional variables and covariates in a complex model increase the amount of cases dropped for missing data and in this instance resulted in an attrition of 81.5%. Though the sample for this analysis (N=2,913) fulfilled the power requirements for the technique used (Peduzzi, Concato, Kemper, Holford, & Feinstein, 1996), a larger valid sample may have produced more robust results. Future replication attempts should take longitudinal attrition into consideration when using retrospective secondary data and in study design for novel tests. ALSPAC has considered several strategies to account for missing data (Fraser et al., 2013; Boyd et al., 2019), including contacting inactive cohort members to invite them to return to the project (Boyd et al., 2012). Replication within the ALSPAC project, utilising child cohort data and children of the child cohort data (Children of the Children of the 90s) could benefit from the contemporary improved data formats and retention the project now maintains.

These results are specific to this population and while ALSPAC can be considered representative of the UK population, valid sample size limitations may

preclude this generalisation. ALSPAC data design and selection were exhaustive in including any variable that could affect or confound any potential studies into their populations and the control covariates used here represented those which were deemed to have the greatest potential effect. With unlimited time and resources, additional covariates would have been included, particularly physical health data, data concerning physical, mental, or social disabilities, and the inclusion of maternal partner variables. Had these analyses been based on a study designed for this purpose, increased covariate measures on a tighter schedule would have potentially produced more valid, reliable results.

In preparing the data for the analyses performed in this chapter, the probabilistic natures of group membership for the prenatal maternal socialisation profiles and psychopathology trajectories were changed to definite membership. It should be emphasised that this was a limitation of the data analysis software and thus a necessary step to perform the final analyses.

7.4.4. Impact and implications

The results of this main effect analysis supported the hypothesis proposing an epigenetic effect between the prenatal maternal social environment and offspring psychopathology in middle childhood. Children primed for specific social environments experienced distress and symptoms of psychopathology in mismatched environments. Their genome had adapted to an environment which resulted in a psychologically maladaptive situation later, as per the prenatal environmental adaptation hypothesis (Lee & Goto, 2013). This study is further support of the epigenetic importance of the prenatal period to later mental health and wellbeing, and its consideration as a contributory factor in mental illness and psychological distress. One criticism of behavioural epigenetics is that, in its few decades as a distinct discipline, it has failed to fully explain the mechanisms by which minor genetic modifications can have mental health outcomes (Carey, 2018), however, the background literature of Rome was not built in a day. Every study examining an epigenetic effect, from a neurological, biochemical, genetic, medical, or psychological viewpoint, contributes to the overall picture of behavioural

epigenetics. This is the most enduring impact of this thesis; another sentence in the library of humanity's understanding of itself.

The implications for policy based on these findings are equally important. As evidence builds in the public consciousness of the health and mental health risks associated with loneliness and isolation (Morin, 2018; Valencia, 2020), further associating those risks with pregnancy would not be hard. As previously discussed, prenatal nutritional guidelines have allowed for the near eradication of many foetal origin disorders in developed nations (Alexander & Kotelchuck, 2001) and an understanding of chemical teratogens has eliminated many formerly common disabilities (Miller, 2004). A scale based on the 5 factors of the prenatal maternal social environment identified in Chapter 2 (*Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support*) could be given during prenatal GP visits to evaluate expectant mothers for isolation just as they would be monitored for gestational diabetes, vitamin deficiency, or any other health issue. Information outlining the dangers of social isolation and loneliness for both mother and foetus could become a routine part of the health advice given to newly pregnant women. With the impact of prenatal social isolation on offspring psychopathology understood, there would exist a greater impetus for prenatal social groups in the community, either in person or digital. The 'clean living' health movement in western culture has focused attention on a more holistic view of mental and physical health and while there are benefits and drawbacks (Engs, 1991; Engs, 2000), the idea of positive prenatal socialisation would fit with this holistic ethos.

The implications for research based on this work and the value to the field come mostly as replication and validation. The body of literature on behavioural genetics is vast and that of behavioural epigenetics is growing quickly. This project has validated theories such as the prenatal environmental adaptation hypothesis and acknowledged the relationship between them and theories which have been the 'pillars' of psychological knowledge for over 60 years, including extraversion personality theory (Eysenck, 1967, 1983), attachment theory (Bowlby, 1969), and ecological systems theory (Bronfenbrenner, 1979). Further, this thesis has functioned as an abstract replication for non-human prenatal stress experiments and human retrospective prenatal stress studies. The results here mirror the effects found in

animal models and human opportunistic samples, warranting the exploration of these hypothesis in further large population longitudinal census-style projects.

7.4.5. Conclusions

The prenatal maternal social environment influenced the psychopathology outcomes of offspring in middle childhood in the ALSPAC child cohort population, as impacted by the child social environment at age 9.5 years. Mothers pregnant while in social isolation gave birth to children who possessed a measure of resilience to the distress of low socialisation but who experienced distress in a highly social environment. Mothers who experienced a highly social prenatal environment gave birth to children likely to experience high levels of socialisation but who suffered distress when in social isolation. It was hypothesised the mechanics of this influence were epigenetic in nature, though this could not be definitively tested with the data at hand.

As ALSPAC is a longitudinal study and the child cohort had passed into adulthood, a logical question would be why examine the proposed effects in middle childhood and not continue to explore psychopathology trajectories and social environments through adolescence? The very nature of adolescence was the barrier in pursuing a protracted effect and deserves a full discussion in light of the results in this chapter.

7.5. Chapter References

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Chapter 8

General discussion

8.1. Introduction

In bringing together the studies that comprised this thesis, this chapter will focus on the findings in context of their place in a wider view of behavioural epigenetics, human adaptation, and mental health. The sections of this chapter will cover evaluating the results of the main hypotheses, discussing these results in the context of socialisation and psychopathology in adolescence, exploring the broader contribution of heritability in psychopathology, looking forward to future work based on this research, reviewing the limitations of the overall thesis, and outlining the clinical/practical impact, implications, and value beyond pure analytical output. This section will cover the relationship between the thesis process and the central thesis hypotheses.

In Chapter 1, it was proposed that the prenatal maternal social environment could affect offspring psychopathology and that this effect was facilitated by epigenetic mechanisms which 'primed' the foetal genome for an expected social environment matching maternal socialisation during pregnancy. This prediction was made based on evidence presented that environmental influences on human health and mental health outcomes are not constrained to the individual lifespan. Further, it was hypothesised that social isolation would constitute a harsh environment necessitating survival-based epigenetic modifications adapting the offspring to the expected harsh social environment. It was expected that children born of socially isolated mothers would feel less distress with low socialisation but suffer increased distress in a highly social environment and that children born of highly socialised mothers would experience high levels of distress when in low socialisation environments. Maternal social isolation exposure *in utero* was hypothesised to have a 'protective' effect against isolation distress. Environmental 'mismatch', an environment radically different from the expected environment, would render offspring behaviour maladaptive and produce increased distress. Psychopathologic symptomology can be described as manifestations of individual distress and therefore the research question was proposed to test the effect of the prenatal maternal social environment on offspring mental health outcomes in middle childhood. To test these hypotheses, data was sourced from the maternal and 1st generation child cohorts of the large population longitudinal study ALSPAC.

The main hypotheses were tested using a series of chronological analyses building upon each other to produce an analytical framework for evaluating the proposed effects by defining and modelling specific environments. Prenatal and historic maternal data was first used in an exploration of the prenatal maternal social environment and how each expectant mother interacted with that environment. Child cohort data was then used to understand the child's experience of socialisation and their expressions of psychopathology across 4 years in middle childhood. Finally, both maternal and child data were used to examine the relationship between prenatal maternal socialisation, child socialisation, and child psychopathology trajectories. These analytical models each quantified an aspect of the main hypotheses, i.e., maternal socialisation was described as a discrete profile determined by factor scores along 5 dimensions of the prenatal maternal social environment. Data were used to represent concepts as statistical models, fitting together like proverbial LEGO blocks in an analytical framework to test a complex research question. Thus, each analysis in this work had value in its circumspect investigation but also contributed to the 'big picture' of the overall thesis, demonstrating the profound effects of an environment on the individual.

The theory of evolution describes the role of distal environments in shaping modern human beings and epigenetic processes illustrate how proximal environments can influence individual health outcomes. The field of behavioural genetics proposes that specific mechanisms underly the heritability of psychopathology and the research of the past several decades has shown the effect of epigenetic processes on psychopathology risk (Tsankova, Renthal, Kumar, & Nestler, 2007; Lester et al., 2011; Nestler, Peña, Kundakovic, Michell, & Akbarian, 2016), while work continues in identifying candidate genes/alleles implicated in mental illness (Jaffee & Price, 2007; Uher & McGuffin, 2007; Farrell et al., 2015). Compared with previous behavioural epigenetic research, this work was ambitious in its scale, eschewing a narrow focus to concentrate on a broader theory of genes and environmental adaptation. This thesis adopted a holistic approach to evolutionary theory, favouring a multi-part model to identify the relationship between various environments and individual outcomes. Exploring the proposed hypotheses was best

accomplished via a complex model rather than by piecemeal studies, providing an analytical framework for future replication attempts or specifically designed studies.

Lastly, Chapter 1 outlined the hypothetical plight of an early *Homo sapiens* female, pregnant and in complete isolation in the wilderness. The cause of her isolation was immaterial but she could have been the sole survivor of disease, conflict, or famine, she may have become involuntarily separated from her people during a nomadic migration, or she may even have been deliberately ostracised and driven out. Over 10,000 years separated her from the women of ALSPAC, but they were linked by mechanisms designed to provide their children with the best possible chance of survival, assuming a harsh life alone. This comparison was made to emphasise the evolutionary influence in the main hypothesis as, in reality, the child born in wild isolation would have had greatly reduced chances of survival compared to the modern offspring cohort. Considerations of humanity's evolutionary journey may not be common in the day-to-day thoughts of contemporary individuals, but its processes are at work in each genome, constantly adapting to increase the chances of survival.

8.2. Thesis Results

This section will cover the overall findings of this work, beginning with an outline of the analytical processes and individual study results, and the results in context of evolutionary and adaptive environmental theory. These findings were important in validating the thesis hypotheses from a behavioural epigenetic standpoint and this section will also discuss the results in relation to genetic contributions to psychopathology outside of the broader body of literature discussed in section 3. This section will also address the results as they apply to a population on the cusp of adolescence, with the challenges of adolescent socialisation and psychopathology discussed in sections 4 and 5. Finally, as environmental parameters featured prominently throughout this work, a final exploration of these as they relate to the findings are included.

The main research question proposed that the prenatal maternal social environment was able to influence child psychopathology by way of subtle epigenetic modifications resulting in behaviours that would be adaptive to the expected environment but maladaptive in other social environments. To test this, the prenatal maternal social environment was statistically modelled and 5 underlying factors, *Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support*, were identified. These dimensions described the environment's main domains and allowed for further testing to understand how a respondent could be described by them and what latent groups existed in the population. The next model identified 3 latent profiles of socialisation within the maternal cohort: High, Low, and a normative Baseline. Having quantified the prenatal maternal social environment and how each mother experienced it through her level of socialisation, the next analysis dealt with modelling the child social environment during middle childhood. This analysis was run to both quantify the socialisation of the child cohort but also to describe their experiences of social interaction at age 9.5 years. This environment was represented as a unidimensional model of Socialisation along which this population varied. The impact of the rate of Socialisation on child distress was determined by measuring symptoms of psychopathology over 4 years, from age 7 to 11 years, and describing the changes over time as 4 distinct trajectories which sub-groups within the population followed: High-Decreasing, High-Stable, Low-Increasing, and Low-Stable. Using the results of these analyses, Chapter 6 pulled them together in a model testing the relationship between the prenatal maternal social environment and psychopathology trajectory dependant on the child social environment.

It was found that the maternal prenatal social profile affected child psychopathology in middle childhood as impacted by child socialisation at age 9.5 years. Specifically, that prenatal maternal isolation led to increasing offspring distress only when the child was in a highly social environment, and that it provided a measure of resilience against the distress of social isolation in middle childhood. High levels of socialisation during pregnancy yielded offspring that when in social isolation, were likely to be consistently highly distressed or experience initially high, decreasing levels of distress. Normative baseline prenatal maternal socialisation produced children following High-Decreasing or High-Stable trajectories only when child socialisation was low. Based on the progression of analyses, from modelling

the prenatal maternal social environment to controlling for the postnatal period, it was evident that members of the offspring cohort born from ‘extreme’ prenatal maternal socialisation profiles suffered distress in social environmental mismatch and this distress was manifested as psychopathology symptomology. These findings validated the thesis hypotheses, which were based on the prenatal environmental adaptation hypothesis proposed by Lee and Goto (2013; Lee, Yamaguchi, & Goto, 2015), offering an epigenetic explanation for psychopathology risk.

At the beginning of this work, it was stressed that while evolutionary theory was central to the epigenetic underpinnings of the thesis hypotheses, this was not a work of evolutionary psychology. Pure survival drive was not the primary or proximal influence on child psychopathology, and that each ‘environment’ the ALSPAC cohort members experienced were complex networks of interconnecting, reactive variables and individuals. While the influence of the prenatal maternal social environment on the offspring genome may have been direct, the effect on offspring behaviour was not. Rather, the drive to survive could be considered a direct influence on the epigenetic mechanisms themselves but only a distal influence on each individual. The difference was important to note, as it is often dismissed as mere semantics in popular culture when considering evolutionary effects on human beings. Evolutionary processes prepare species for their environment but cannot predict the intricacies of those environments (Lòpez-Maury, Marguerat, & Bähler, 2008; Bell & Gonzalez, 2011).

The delta between epigenetic expectation and reality was best illustrated by the extreme populations in both cohorts, but the results concerning the moderate populations were also illuminating. The normative Baseline Socialisation profile was the 36% of the maternal population, the closest to a population mean, and were described by consistent levels of all 5 socialisation dimensions, though on a lesser scale than the High Socialisation profile. This group was used as the reference category in comparing significant predictors of Low/High profile membership. The 2nd Socialisation tertile of the child population experienced a moderate level of socialisation and were not predicted to experience significant distress as result of that environment. The children of Baseline Socialisation profile mothers had no ‘extreme’ epigenetic expectations of their environment, experiencing no distress

when highly socialised and high-decreasing distress in a moderate social environment. Only social isolation produced significant, lasting distress for this sub-sample, demonstrating that while neither extreme of socialisation was expected, the moderate categories were closer to the highly socialised categories than the isolation categories.

It is without doubt that environments are capable of informing specific phenotypes which in turn influence the lives and health outcomes of individuals (Bateson et al., 2004). This thesis identified 3 ‘social phenotypes’ in the child cohort and tested the interactions between them and the child social environment to determine how they influenced mental health outcomes, theorising that the prenatal maternal social environment informed the phenotypic expression of child behaviour which would in turn affect child socialisation and their social environment. While the prenatal maternal social environment affected reaction to distress as represented by psychopathology in middle childhood, the child social environment was the lynchpin of that reaction while also having been influenced by the prenatal maternal social environment. This model supports phrasing the finding as ‘social phenotypes’ as the offspring from differing prenatal social environments had resultant differing socialisation and psychopathology trajectories independent of other contributory factors.

These results have been described using the language of epigenetics, but they also directly relate to the study of genetics and heritability as contributors to psychopathology risk. As understanding of genetic legacy has broadened over more than a century, so too has behavioural genetics come to inform more popular understandings of psychopathology. The idea of a genetic factor in mental illness has reduced stigmatic beliefs around personal responsibility for the illness but increased beliefs of genetic predetermination concerning the individual and family members (Phelan, Cruz-Rojas, & Reiff, 2002; Phelan, 2005; Rüsch, Todd, Bodenhausen, & Corrigan, 2010). The findings here introduce an environmental component to this ‘mix’, offering the potential for new avenues of public perception of psychopathology and possibly working to erode harmful views of genetic predetermination. Viewing mental illness as the result of specific interactions rather than ‘afflicted bloodlines’ could work to dilute stigma. In addition, multiple studies

have confirmed that psychosocial variables are still seen as largely responsible for mental illness, despite genetic components (Read & Harré, 2001; Read, Haslam, Sayce, & Davies, 2006; Schnittker, 2008), meaning that acceptance of adaptive epigenetic risk may be possible due to the impact of those psychosocial variables on specific environments.

This project concentrated on psychopathology in middle childhood up to the threshold of adolescence and a natural question would be, why not continue longitudinal modelling of socialisation and psychopathology through adolescence? While data existed on both constructs throughout adolescence and beyond, the specific measure used to model socialisation was only given at 9.5 years and the SDQ was only used until 11 years. As repeat measure data for these scales did not exist in adolescence, an analysis attempting to compare socialisation and psychopathology using proxy measures would have been fundamentally flawed and statistically invalid. The decision to examine the socialisation-psychopathology relationship in middle childhood was partially based on data availability but also due to the qualities of the developmental period itself, as the dynamic development of early childhood was complete and the physiological and psychological upheaval of adolescence was not yet underway. With the individual developmental changes endemic to puberty and the multiple environmental changes inevitable with the passing of time, it was very likely that the child cohort experienced change in both socialisation and psychopathology during adolescence. While charting and analysing that change and its implications was not possible in this work, the results here laid the groundwork for the design of such research.

One final concept should be considered when understanding the thesis results, and is that in the absence of concrete biological evidence of epigenetic modifications, the effect of the prenatal maternal social environment on offspring psychopathology is the consequence of an aggregate of interacting factors exerting influence on both the mother and child. Environments, environmental factors, and environmental parameters featured prominently in the supporting theories and stated hypotheses of this work, and the results have furthered understanding of environmental interactions. It is possible that the socioeconomic, demographic, environmental, and personal variables which influenced maternal prenatal

socialisation persisted, either directly or indirectly, to interact with the multitude of variables which influenced child socialisation and psychopathology risk. This longitudinal 'macroenvironment', itself a network of reciprocal factors, could be thought of in terms of risk load on the individual; a structure bearing too much weight will eventually buckle while the one with little burden will remain sturdy. Generational cycles of poverty, discrimination, and isolation exemplify the longitudinal nature of these issues, combined with genetic contributions and the effects of familial mental illness in families. Again, until these results can be validated in the ALSPAC epigenome, this 'macroenvironment' remains a possibility.

8.3. Genetic Contributions to Psychopathology

While this thesis has concentrated on epigenetic modifications, the activation or deactivation of genes in response to the environment, they are far from the sole connection between the personal genome and psychopathology risk. The idea of heritability in psychopathology was common in the ancient world, from Greece (Blue, 1993) to Mesopotamia (Nemet-Nejat, 1998) and Indo-China (Fàbrega, 2001), even if mental illness was attributed to a variety of speculative causes. Traits persisting in a family line are now understood to be heritable, either through direct Medelian inheritance or more complex interaction between genes and the environment, which influence trait expression. Genetics cannot be thought of as predestination in the context of human behaviour; while a mutation on a specific gene in a specific location might always produce a specific medical pathology, there is no causal gene 'for' anxiety, depression, or psychosis, which expresses with 100% certainty. Genetic contributions to psychopathology should not be ignored, rather conceptualised as risk. As an example, a candidate gene affecting sensitivity of the HPA axis could mean increased reactivity when combined with environmental stressors which, under specific conditions, could lead to an individual experiencing symptomology and distress. Discussing genetic risk as a factor alongside environmental and socioeconomic risk both demystifies and legitimises it as a contributor.

Bringing together genetic legacy, lived experiences, and environmental factors, the biopsychosocial model of mental illness acknowledges the interplay between them in a risk model. Many variables discussed in the current and previous chapters affect that risk but none of them, either alone or in concert with others, are direct causal factors of psychopathology (Jones et al., 2018). Differences in risk may be responsible for differences in psychopathology expression; if two individuals encounter the same trauma and the one continues on as usual while the other develops PTSD, what differences led to that outcome? Starting with physiology and personal variables, the most varied and personal is the genome and its interactions with every environment the individual will encounter. In exploring the similarities and differences of the individual genome, genome-wide association studies (GWAS) are used to examine the entire genetic codes of a given population, either in a census-style 'sweep' or targeting a clinical population, usually compared against a control (Monolio, 2010). These studies catalogue single-nucleotide polymorphisms (SNPs), specific location substitutions which constitute the most general genetic variants (Pearson & Manolio, 2008).

It is by now well established that genetic inheritance is a significant contributor to psychopathology risk, both in terms of overall polygenic risk score and specific candidate genes. A polygenic risk score is an aggregate measure used to describe phenotypic effect from multiple contributing alleles when none have a significant individual effect and this score is derived from phenotype-gene correlations from GWAS and calculated in a weighted regression (Dudbridge, 2013). The regression coefficient for any given trait can be used to predict phenotypic expression and is used in humans to predict disease/mental illness susceptibility, health outcomes, and individual biochemical interactions (Richardson, Harrison, Hemani, & Smith, 2019). Whereas a polygenic risk score is calculated based on multiple genetic variants in a large population, the candidate gene approach assumes the association between a specific gene and phenotypic outcome based on previous research (Zhu & Zhou, 2007), and searches for that gene's variants in a population. This approach allows for the consideration of multiple variants' effects on expression and the potential for a dose-response relationship with the outcome (Tabor, Risch, & Myers, 2002). It is important to note that psychopathologies have complex genetic fingerprints involving multiple gene and variant combinations (de

Jong et al., 2018) which describe risk and potential vulnerability to environmental variables (Duncan & Keller, 2011). These compound phenotypes have been implicated in anxiety (Costas et al., 2010; Purves et al., 2019), depression (Howard et al., 2018; Ormel, Hartman, & Snieder, 2019), psychosis (International Schizophrenia Consortium, 2009; Fromer et al., 2016), and other common psychopathologies (Neumann et al., 2016; Brikell et al., 2018).

Vulnerability is also an appropriate term to use when describing genetic risk in psychopathology, referencing the diathesis-stress model of mental illness in gene x environmental interactions and correlations (Rende & Plomin, 1992). This model conceptualises the compound effect of various contributory variables as a latent vulnerability, only realised once a stressor, or multiple stressors, overwhelm the individual. Much of the public understand this as environments or events that cause people to 'snap' with a sudden onset of psychopathology symptoms (Schomerus et al., 2012; Johnson & Miller, 2016). Belsky and Pluess (2009) suggest that the diathesis-stress model could be more accurately described as differences in plasticity rather than vulnerability, reflecting an individual's reactivity to environmental factors, with several 'plasticity' genes implicated (Belsky, Jonassaint, Pluess, Stanton, Brummett, & Williams, 2009). A propensity for being affected by these factors, unknown until encountering such a factor, like trauma, is the perfect representation of the diathesis-stress model. Epigenetic mechanisms have been previously found to be associated with glucocorticoid receptor gene modifications in victims of child abuse (Heim & Binder, 2012), as well as being associated with risk of depression (Klengel & Binder, 2013), suicidality (Mann & Currier, 2010), and other common psychopathologies (Klengel & Binder, 2015). The additional risk of prenatal contributory factors could be seen as support for the diathesis-stress model.

Beyond the multi-gene effect of polygenic risk, several specific candidate genes have been implicated in and investigated for direct influence in psychopathology risk. The transmembrane protein *TMEM132D* has been associated with panic disorder (Shimada-Sugimoto et al., 2016), anxiety (Erhardt et al., 2012; Howe et al., 2015), and anxious symptoms in depression (Erhardt et al., 2010). The neurotransmitter modifier gene *COMT* has variants identified as major contributors to psychosis (Gothelf et al., 2005; Niarchou, Zammie, Escott-Price, Owen, & van

den Bree, 2014) and anxiety (McGrath, Kawachi, Ascherio, Colditz, Hunter, & De Vivo, 2004; Stein, Fallin, Schork, & Gelernter, 2005), as well as mediating the effect of some antidepressants (Baune et al., 2008; Benedetti, Colombo, Pirovano, Marino, & Smeraldi, 2009). Additionally, the gene *MAOA*, which encodes the neurotransmitter regulation enzyme monoamine oxidase A, has been called the 'warrior gene' and is associated with aggression (Buckholtz & Meyer-Lindenberg, 2008; McDermott, Tingley, Cowden, Frazzetto, & Johnson, 2009) and environmental interactions with child abuse and maltreatment resulting in psychopathology (Kim-Cohen et al., 2006; Byrd & Manuck, 2014).

As is evident, pure Mendelian inheritance does not account for the association between polygenic phenotypes or specific candidate genes and psychopathology risk. With direct inheritance, that which is harmful is usually bred out of a species (Lacy, 1997; Loewe & Hill, 2010) unless the benefit of its causal mechanism outweighs that harm. Sickle cell disease in humans is a prime example of a genetic benefit (resistance to malaria) which results in pathology when both copies of the inherited gene are affected (Serjeant, 2010). Individuals experiencing severe, long-term psychopathology, especially psychosis, may have a reduced life span or be party to fewer reproductive opportunities (Nanko & Moridaira, 1993; McGrath, Hearle, Jenner, Plant, Drummond, & Barkla, 1999), lessening the chance for direct inheritance. Polygenic inheritance depends on the contributors from both sides of the chromosome, introducing exponential variance past the first generation (Fernando, Stricker, & Elston, 1994). A genotype is not a guarantee of an outcome, and it has become apparent over the past several decades that genetic risk of psychopathology represents not only the genes in question, but also the gene x environment interaction (Rutter, Moffitt, & Caspi, 2006; Thapar, Harold, Rice, Langley, & O'Donovan, 2007).

Genetic contributions to psychopathology outcomes highlight the importance of the environment and epigenetic changes that result from environmental interactions. A foetal genotype already carrying a high polygenic load for mental illness would incur additional risk when modified for an environment it will not face in life, adding maladaptive behaviour and environmental mismatch to total individual risk. Additionally, psychosocial variables which increased risk for one

generation (poverty, discrimination, national conflict, etc.) may persist in the offspring's environment, further perpetuating a cycle of distress.

8.4. Adolescent Socialisation

Taken in context with a changing social and personal identity and a brain not fully able to manage this distress, it is hardly surprising that adolescent social isolation can be damaging to self-esteem while also impacting identity (Laursen & Hartl, 2013). Adolescence, a developmental period qualified as ages 10 to 19 years (World Health Organisation, 2014) and encompassing puberty, is a crucial time of physical, cognitive, and emotional development. It is also a liminal, transitional time when the sphere of individual identity influence shifts from parents/family to peers/friends (Tanti, Stukas, Halloran, & Foddy, 2011). This pulling away is potentially rooted in evolutionary adaptation, with social species relying on group dispersal to avoid inbreeding (Pusey, 1987; Wolff, 1997), keep groups to manageable numbers (Matthysen, 2012), and for greater reproductive success (in non-human mammals: Dobson, 1982; Wolff, Lundy, & Baccus, 1988; in humans: Kramer, Schacht, & Bell, 2017). Dispersal in social mammals usually occurs at the point of reproductive maturity (Wolff, 1994) and in this, humans do not significantly diverge (Clarke & Low, 1992; Kramer 2014). Humanity's success in transitioning away from a predominantly nomadic, scavenger lifestyle has eliminated the need for group dispersal as most cultures have taboos against incest/inbreeding (Bischof, 1972), most habitable areas can provide for the populations (though this is rapidly changing due to climate change and global inequity), and there is no longer the need for every available human to reproduce to ensure species survival. It must be noted, however, evolutionary pressures constitute distal influences and do not directly produce individual behaviour.

The advent of puberty in humans signals the beginning of reproductive maturity and coincides with rebellious behaviour and attitudes (Abrahamson, Baker, & Caspi, 2002; Luthar & Ansary, 2005). Adolescent changes in attitude reflect a shifting of identity as a result of both maturation and a widening social environment, with exposure to attitudes and world views that may differ from their family

environment (Kroger, Martinussen, & Marcia, 2010). With greater mobility (both literal and social) and better capacity for social cognition, the shift from family to peer influence can be highly beneficial. Personal identity is in a state of reinvention during adolescence, open to influence from peers, and an individual's social identity is affected by their new company (Tanti, Stukas, Halloran, & Foddy, 2008; Jones, Vaterlaus, Jackson, & Morrill, 2013). Social groups convey group benefits, including in-group favouritism, values, and solidarity with members versus out-group individuals (Tarrant, North, Edridge, Kirk, Smith, & Turner, 2001; Tarrant, 2002). The adolescent's new attitudes, values, and maturing identity may conflict with the family environment, particularly with parents not ready to cede their influence, and the new social environment can replace that emotional security, proving a secure base and fulfilling the biological need for social interaction.

Physical brain development plays a substantial role in these changes via the growth and refinement of the 'social brain', producing social flexibility (Blakemore, 2008, 2012; Nelson & Guyer, 2011), emotional, and cognitive development. The medial prefrontal cortex (MPFC), centre of social evaluation and social judgement, increases in volume during adolescence, and this area indicates arousal during social engagement and processing of social emotion (Burnett, Bird, Moll, Frith, & Blakemore, 2009; Somerville, Jones, Ruberry, Dyke, Glover, & Casey, 2013). This region is also important in self-regulation (van Noordt & Segalowitz, 2012) and predictive response-based behaviour (Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004). Maturation and cortical thickening of the MPFC continue into early adulthood and follow trajectories suggesting both genetic and environmental influences (Mills, Lalonde, Clasen, Geidd, & Blakemore, 2012). Thus, adolescents have increased drive to socialise outside of the family, more mobility in opportunity, and are becoming better at doing so.

Socialisation offers a wealth of benefits to the individual adolescent (Stanton-Salazar & Spina, 2005). Peer socialisation provides emotional support which can strengthen emotional self-regulation (Farley & Kim-Spoon, 2014; Miller-Slough & Dunsmore, 2016), as well as social competency (Dodge, Pettit, McClaskey, Brown, & Gottman, 1986; Pickard, Happé, & Mandy, 2018) and positive adjustment via co-rumination (Rose, Carlson, & Waller, 2007). Cheng and Furnham (2002) found peer

friendship a predictor of self-reported happiness, and there is a wide body of literature exploring the relationship between positive social experiences and adolescent self-efficacy (see Connolly, 1989 for review). Peer groups can reinforce individual identity (Pugh & Hart, 1999) and relational and individual identity largely influenced by peers over family (Meeus & Dekoviíc, 1995). Social connectedness and higher peer status in adolescence are associated with better physical health outcomes (Almquist, 2009; Mundt & Zakletskaia, 2014) while positive peer interactions protected individuals from social anxiety (La Greca & Harrison, 2010) and depressive symptomology (Ueno, 2005). Positive peer interactions were also associated with better mental health outcomes in adulthood (Hightower, 1990; Östberg, 2003; Bond et al., 2007).

The danger of social isolation in adolescence is the limited ability of the growing brain to deal with isolation, which in adolescence is usually due to deliberate ostracism/social exclusion. The maturing social brain of the adolescent is still learning how to manage the distress of isolation, with greater susceptibility to the promise of social reward over risks incurred (Sebastian, Viding, Williams, & Blakemore, 2010). Interpersonal competency in regulating the rejection distress of isolation varies along individual differences but the involved neurological and cognitive mechanisms are diffuse across the brain (Masten et al., 2009). Whereas social isolation has physiological and psychological consequences on its own, in adolescence it has the additional dimension of ostracism. An adult may be socially isolated for any number of reasons, but greater mobility and resources mean wider choice in socialisation where adolescents are more confined to smaller social environments. While a small percentage may be choosing to self-isolate (Young & Bradley, 1998), the majority of social isolation in adolescence is either brief or chronic ostracism (Leets & Sunwolf, 2005; Newman, Holden, & Delville, 2005), encompassing elements of rejection and social exclusion (Williams, 2007) which compound distress.

Due to the rapid social, cognitive, and emotional growth occurring during adolescence in addition to mercurial individual social environments, it was decided that testing the thesis hypothesis during adolescence with the ALSPAC data available would not produce robust results. While it was natural to speculate on the

child cohort social environment in adolescence and how it may have differed/mirrored the child social environment, a valid statistical comparison could not be made. However, the 8-item scale used to model Socialisation at age 9.5 years was not strictly age specific and could be used in future work to the same degree with adolescents (potentially substituting 'kids' with 'teenagers' in each item) in a true longitudinal test of the main hypothesis. Further studies based on these results might make use of the adult data now available for the child cohort, examining Socialisation at age 9.5 years against socioeconomic, mental, and physical health outcomes, or even in the second generation of ALSPAC, Children of the Children of the 90s.

8.5. Adolescent Psychopathology

The hormonal effects of puberty, changes in brain physiology, liminal identity, and potential low socialisation or shifting socialisation all increase the risk for mental illness symptomology during adolescence. Generally considered to be a 'turbulent' time (Rutter, Graham, Chadwick, & Yule, 1976), adolescence would be better conceptualised as a transitional stage of development. Physiologically, puberty processes are underway as the body increases production of androgens and associated hormones with an end-goal of physical and reproductive maturity. Cognitive development is also ongoing, and though an individual cannot be said to be fully cognitively mature until approximately age 25 (Arain et al., 2013), their brain grows in size and complexity between the ages of 10 and 19 years. While some psychopathologies are common/have their advent in childhood (Merikangas, Nakamura, & Kessler, 2009; Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015), many individuals with no previous psychopathologic symptomology develop a mental illness during adolescence (Zahn-Waxler, Shirtcliff, & Marceau, 2008). The prevalence rates of psychopathology in adolescence vary by type of disorder and other factors, as explored in Costello, Copeland, and Angold (2011) who reviewed adolescent mental health studies between 1997 and 2011. Estimates based on the World Health Organisation World Mental Health Survey Initiative (Kessler, Haro, Heeringa, Pennell, & Ustün, 2006) found the onset of approximately 50% of primary mental disorders in adolescence (Kessler, Amminger, Aguilar-Gaxiola, Alonso, Lee,

& Ustün, 2007). Analysis based on the World Health Organisation Atlas Project (World Health Organisation, 2005) also showed that half of adult/lifetime mental disorders began in adolescence with 20% of the child/adolescent population living with psychopathology (Belfer, 2008).

The 2 main biological processes ongoing during adolescence, hormonal puberty and brain development, are both implicated in psychopathology risk. Gonadal steroid hormones are pivotal in neural restructuring and are present in the bloodstream at elevated levels during puberty, secreted by the activated hypothalamic-pituitary-gonadal (HPG) axis (Sisk & Zehr, 2005). These hormones also impact key neurotransmitters, including dopamine (Sinclair, Purves-Tyson, Allen, & Weickert, 2014), with dopamine dysregulation implicated as a contributor to several psychopathologies (Herbert, 1997), specifically schizophrenia (Laruelle, Kegeles, & Abi-Dargham, 2003; Kapur, Mizrahi, & Li, 2005; Seeman et al., 2005). Overall activity and sensitivity increase in the hypothalamic-pituitary-adrenal (HPA) axis, crucial in physiological stress response (Walker, 2002), with increased response in social and emotionally reactive situations (Dahl & Gunnar, 2009). Chronic over-stimulation of the HPA axis is associated with increased psychopathology risk (Lupien, McEwen, Gunnar, & Heim, 2009; Roberts & Lopez-Duran, 2019) with generalised symptomology and pubertal timing differing by gender (Hayward & Sanborn, 2002; Graber, 2013).

Brain development during adolescence is as significant as that in early childhood, with a neurobiological reorganisation affecting every aspect of cognition (Keshavan, Geidd, Lau, Lewis, & Paus, 2014). Brain plasticity is at its peak (Lee et al., 2014) and allows for growth and maturity of brain structures, increase in brain volume and white matter (Walker, 2002), synaptic pruning and efficient restructuring of neurochemical pathways (Keshavan, Geidd, Lau, Lewis, & Paus, 2014), and development of the networks and structures comprising the ‘social brain’ (Burnett, Sebastian, Kadosh, & Blakemore, 2011). Trauma and stressors (adverse events, poverty, abuse/neglect, etc.) can impede health brain development during adolescence (Casey et al., 2010; Fuhrmann, Knoll, & Blakemore, 2015), increasing risk of psychopathology (Cook et al., 2005). During adolescent development, inborn defects or genetic abnormalities may express as the brain matures (Walker, 2002),

leading to or worsening symptomology. As in middle childhood, self-regulation processes are still maturing (Moilanen, 2006; Gestsdottir & Lerner, 2008) and self-regulation can be instrumental in mediating distress (Parto & Besharat, 2011) as well as acting as a protective mediator against psychopathology (Baker & Hoerger, 2012; Palacios-Barrios & Hanson, 2019).

Both the experience and expression of distress as psychopathology symptomology can have detrimental effects on socialisation. An adolescent experiencing mental distress may face stigma from their peers or educators (Corrigan, Lurie, Goldman, Slopen, Medasani, & Phelan, 2005; O'Driscoll, Heary, Hennessey, McKeague, 2012; Kaushik, Kostaki, & Kyriakopoulos, 2016), resulting in further distress and isolation (Moses, 2009). Self-stigma, or distress over their mental illness is also a factor in loss of self-esteem and self-efficacy (Corrigan, Watson, & Barr, 2006; Mukolo, Heflinger, & Wallston, 2010). Even without stigma, many psychopathologies are associated with social withdrawal in children/adolescents (Rubin, Coplan, & Bowker, 2009), specifically, depressive disorders (Allen, Insabella, Porter, Smith, Land, & Phillips, 2006; Katz, Conway, Hammen, Brennan, & Najman, 2011), anxiety disorders (Schneider, 2009; Biggs, Vernberg, & Wu, 2011), and psychosis (Cullen, Guimaraes, Wozniak, Anjum, Schulz, & White, 2011; Mäki et al., 2014). Support from peers can mediate distress (Vilhjalmsson, 1994; Pössel, Burton, Cauley, Sawyer, Spence, & Sheffield, 2017) and those who withdraw due to mental illness symptomology may be cutting themselves off from that support. The adolescent's family may react negatively to their distress, either contributing to stigma (Hinshaw, 2005; Moses, 2010a, 2010b) or by withholding support/preventing access to mental health services (Hinshaw, 2005), and both are associated with poor mental health outcomes (Lambert et al., 2013). Concern over future outcomes and loss of adult potential may also constitute a significant stressor, playing into the self-stigma and fear related to a 'mental health patient' or 'service user' label (Hinshaw & Stier, 2008).

As discussed above, adolescent relationships change and the balance of influence shifts away from the former base of parents/family. This transition can be difficult, especially if parents are not ready to accept a lesser role in their child's life, but also if the adolescent shifts away from family and has no peers to replace them.

The individual can be imagined as a small boat newly unmoored from the dock and if unable to find a new mooring, it risks being swept away by a dangerously swift current (Nathanson & Roth, 2019). With no secure base to provide positive socialisation, feelings of security, and emotional fulfilment, an adolescent can become isolated, dealing with both the distress of adolescence and lack of socialisation alone. These constitute considerable stressors which can contribute to the risk of mental illness and erode mental wellbeing (Grant, Compas, Stuhlmacher, Thurm, McMahon, & Halpert, 2003). In addition, lack of a secure base can be distressing, as adolescents who cannot rely on parents to fill that need turn to peers (Nickerson & Nagle, 2005).

The reciprocal relationship between social isolation and psychopathology was first explored in the context of prenatal socialisation in Chapters 2 and 3, then discussed in the context of middle childhood in Chapters 4 and 5, and finally reviewed in the context of adolescence in this chapter. While this relationship could not be investigated in the ALSPAC cohort during this project, there are several basic predictions that could be made in imagining the 4 psychopathology trajectory classes in adolescence. The first is that, assuming no significant environmental or personal changes, the individuals experiencing low levels of distress at the end of middle childhood (Stable-Low and High-Decreasing trajectories) were able to continue socialising at a level meeting their personal socialisation needs. The second is that, again assuming no changes, those experiencing high levels of distress (Stable-High and Low-Increasing trajectories) endured social isolation either from social withdrawal or social ostracism/exclusion, with stigma being a potential factor. It would also be hoped that, given the nature of socialised healthcare in the UK, those individuals experiencing distress received timely intervention and appropriate treatment.

The adolescent version of the SDQ features slightly different wording and has been utilised in populations between the ages of 11 and 16 years (Goodman, Meltzer, & Bailey, 1998). If the SDQ had been repeated throughout adolescence in the ALSPAC child cohort, psychopathology trajectories could have been modelled using the same latent growth mixture model technique used in Chapter 5, followed by a latent transitional analysis to identify any change in trajectory between middle

childhood and adolescence. Further covariate analyses could then have determined which variables identified change or stability in trajectory, deepening the understanding of how the prenatal maternal social environment affected child mental health outcomes. Though not available for the scope of this project, this presents the opportunity for prospective longitudinal studies to exploit such a design and capture the 'whole story' of psychopathology from middle childhood through adolescence.

8.6. Future Directions

The work of this thesis and the results represent the starting point for a host of future works including potential validation of findings via the use of ALSPAC bio-data, replication trails in other large population census-style data sets, and further studies into social isolation in the child (now adult) Children of the 90's cohort. This section will be a brief overview of possible future avenues of study made possible by this project.

As discussed above, methylation and genome data exist for both the maternal and child cohort, opening up the possibility for biological validation of these results. A GWAS conducted with a clinical population (offspring of Low Socialisation profile mothers) compared against a control population (offspring of High Socialisation profile mothers) could identify SNPs differences potentially associated with maternal social isolation during pregnancy. A potential limitation could be the availability of data from the sub-populations, as not all members of the cohort attended physical data collection clinics (Boyd et al., 2012; Fraser et al., 2013), but even a small study could yield results of sufficient value to propose launching an independent designed study. The goals and aims of such a study would be primarily to test the hypothesis that prenatal maternal social isolation has a direct epigenetic effect on offspring which impacts on mental health outcomes in middle childhood dependant on the child social environment, but also examining the 'macroenvironment' of maternal influences on the prenatal maternal social environment and family environmental factors. An epigenetic modification is the result of a gene x environment interaction, but such interactions occur constantly throughout the lifespan, leading to the possibility that the prenatal maternal social

environment is only a mid-step in the process resulting in the offspring mental health outcome.

The use of population genomic data for GWAS research has enabled identification of genetic variants associated with various health and mental health outcomes, and once identified, the SNP can be 'searched for' in other datasets. Additionally, techniques now exist to identify multiple phenotypes within a GWAS (O'Reilly et al., 2012), simplifying research where several SNPs might be contributors to a specific outcome. Isolating the phenotype markers and variants associated with the expressions found in this thesis could mean establishing a genetic based framework for understanding variation in individuals, particularly in personality and psychopathology expression. Many GWAS catalogue databases are open-access with results readily available through a host of online open-source user interfaces (Ramos et al., 2013; Welter et al., 2013), boosting the ability of researchers to share results and design follow-up studies. Horwitz, Lam, Chen, Xia, and Liu (2018) reviewed 10 years of psychiatric GWAS research and SNP identification, noting the complex nature of some psychopathologies, specifically schizophrenia, which had 74 associated SNP replications. Exploring the specific prenatal maternal social environment dependent phenotypic variants associated with expressed behaviour could change the understanding of individual differences and personal variance in socialisation and the relationship between socialisation and psychopathology.

These results were present in the ALSPAC population, thus, the UK population from the 1990s through the early 2000s and cannot be generalised further. Replication must be the next step in ascribing an epigenetic explanation for the results and a vital step in proposing the potential universality of this effect. Exploiting large population datasets from other countries and testing the main hypotheses via comparable studies would fulfil both replication requirements and the ability to generalise to other cultural populations. For example, the Western world is largely individualistic while Eastern cultures are far more collectivist (Earley, 1993) and these differing cultural norms could yield unique results when modelling the prenatal maternal social environment, child Socialisation, or how psychopathology is quantified (Triandis, 1996). In the ALSPAC maternal cohort, the prenatal maternal

social environment was modelled along 5 dimensions, *Trust*, *Contact*, *Sharing*, *Primary Support*, and *Secondary Support* with distinct profiles differing by factor score. While the dimensions would remain consistent if the 13-item social support/networking scale were used, the high/low/baseline profiles could differ along them, based on cultural norms. A child in a collectivist society may have differing views of themselves as a social being when completing the 8-item socialisation scale, and while the SDQ has been validated for cross-cultural use (Woerner et al., 2004), it should not be used to compare cultures (de Vries, Davids, Mathews, & Aarø, 2017), meaning psychopathology trajectories would need to be interpreted in their own context. Replication attempts in additional populations should be the logical next step towards higher generalisation.

SARS-CoV-2 emerged during the undertaking of this thesis and the resultant COVID-19 pandemic saw billions worldwide forced to quarantine, self-isolate, or practice social distancing via state-mandated lockdown. For an unknown percentage of the world's population, that meant living in partial or abject social isolation. ALSPAC continued remote data collection during this time (University of Bristol, 2020a), including surveys specific to COVID-19 in terms of physical health and mental wellbeing of the Children of the 90s cohort during lockdown in the UK (University of Bristol, 2020b; 2020c). Such data could prove vital in understanding the relationship between the prenatal maternal social environment and offspring psychopathology in adulthood, specifically concerning offspring social isolation. Data used in this project captured adolescent offspring socialisation as influenced by a multitude of factors, some of which contributed to social isolation. Whereas deliberate isolation research is highly unethical, lockdown conditions have inadvertently provided an opportunity to explore themes of this thesis in a 'captive' population and there is precedent for exploiting such events (Project Ice Storm, the Queensland Flood Study, the Dutch Famine Winder study, etc.) As ALSPAC is a generational study, future work concerning this cohort will exploit the COVID-19 data in an 'epilogue' study carrying on from this project's findings.

8.7. The Prenatal Maternal Social Environment and Psychosis

While this thesis considered psychopathology in the broadest sense of distress and common symptomology, additional longitudinal data was sourced detailing the experiences of psychotic-like events throughout adolescence. While there was a vast body of literature supporting a survival-based, evolutionary connection between prenatal social stressors, epigenetic adaptations, and generalised mental health outcomes, the research concerning adaptive psychosis was not as plentiful. Diagnostics have moved consistently away from considering a singular disorder ('schizophrenia') and towards psychosis as a state with dimensions that can manifest in a variety of ways (Dutta, Greene, Addington, McKenzie, Phillips, & Murray, 2007; Linscott & van Os, 2010; Tandon et al., 2013). The case has been made previously of the relationship between specific psychosis symptomology and evolutionary theory (Polimeni & Reiss, 2003). Burns (2006) argues that psychosis is an unfortunate "*by-product*" of the evolution of the social brain, acknowledging the important aspect of social interaction for survival, with Kelleher, Jenner, and Cannon (2010) concluding in their review that adaptive advantage and survival lie at the centre of the most likely evolutionary theories of psychosis. Polygenic risk acknowledges the net effect of several genes associated with psychosis and it has been suggested that these genes are associated with vital benefits, such as creativity (O'Reilly, Dunbar, & Bentall, 2001; Kozbelt, Kaufman, Walder, Ospina, & Kim, 2014) and intelligence (Kéri, 2009). While psychosis risk may be influenced by the individual genome, it is possible that the symptomology of psychosis has survival-based roots.

Isolation is a deficit environment and one known to produce auditory and visual hallucinations in extremity (Ziskind, 1958; Zubek, Pushkar, Sansom, & Gowling, 1961; Kellerman, Rigler, & Siegel, 1977; Grassian, 1983; Haney, 2003). As a starving body breaks down its own muscle and connective tissue to survive, so also it seems that the brain in severe isolation produces its own stimuli. It has also been theorised that hallucinations are a misattribution of input (Costafreda, Brébion, Allen, McGuire, & Fu, 2008; Brookwell, Bentall, & Varese, 2013) and in primal situations of hypervigilance, it was more advantageous to react to all stimuli rather than ignoring a potential threat (Dodgson & Gordon, 2009). In times of increased

stress and distress, hypervigilance could lead to misattribution of normative stimuli as hallucinatory stimuli, state Dodgson and Gordon (2009). In prehistoric times, isolation was tantamount to death and finding other humans meant an increased chance of survival, so hypervigilance for signs of others, especially the human voice, could be considered adaptive for a child born into isolation. It is possible such an epigenetic modification could increase the risk of auditory hallucinations. Following from the results here, investigating the potential association between a low socialisation prenatal maternal social environment and hallucinations in the ALSPAC child cohort is a natural progression.

Considering the dangers of being born into isolation, paranoia is a very useful state for a human being alone in the wilderness under constant threat (Raihani & Bell, 2019), but it is maladaptive in most contemporary settings. In situations of low socialisation due to ostracism during pregnancy, the resultant child may face a hostile social environment where being paranoid of others is a matter of survival (Green & Phillips, 2004). Delusional thought may not match reality, but its mechanisms and processes may reveal the adaptive functioning roots of thought development (McKay & Dennett, 2009). Creative thinking and pattern cognition would have been valuable to an individual living in isolation, and those abilities are associated with delusion risk (Butler & Braff, 1991; Kéri, 2009). Hallucinations, paranoia, and delusions are not the only major symptomology of psychosis, but they are highly prevalent (Kendler, 1996; Johns et al., 2004; Spikol & Murphy, 2019) and are not always indicative of psychotic disorder (Kelleher, Connor, Clarke, Devlin, Harley, & Cannon, 2012; Linscott & van Os, 2013).

These symptoms may constitute dormant cognitive mechanisms of evolutionary value with the potential to be re-engaged in times of threat, stress, and distress, becoming highly maladaptive in a normative setting (Cariaga-Martinez, Gutiérrez, & Alelú-Paz, 2018; Scheepers, de Mul, Boer, & Hoogendijk, 2018). As with generalised psychopathology, it is possible that the prenatal maternal social environment, specifically prenatal social isolation, could result in specific epigenetic modifications which increase the risk for psychosis symptomology by priming the foetal genome for an environment where such survival mechanisms would be necessary. Manifestations of psychosis vary widely between individuals (Jablensky

et al., 1992; Tsaung, 2000), introducing the possibility of a variance in methods of onset (Raiji, Ismail, & Mulsant, 2009; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009), agreeing with the concept of a 'psychosis phenotype' existing in a spectrum in the population (van Os, Hanssen, Bijl, & Ravelli, 2000). Expression of psychotic symptomology by an individual usually garners negative attention from society (Norman, Windell, Lynch, & Manchanda, 2011; Yang, Anglin, Wonpat-Borja, Opler, Greenspoon, & Corcoran, 2013), with stigma increasing distress, perpetuating the threat to survival, and potentially creating a worsening psychotic state. The results of this thesis justify examination of the effects of the prenatal maternal social environment on psychotic symptomology with an eye towards the aforementioned holistic evolutionary approach.

8.8. Thesis Limitations

While the results and implications of this thesis are exciting, they must be taken in part with the limitations present. All analyses were based on secondary data, some nearly 30 years old and all variables had some degree of missingness. ALSPAC collected data under the auspices of its mission statements and these data were retrospectively used to explore the thesis hypotheses investigated here. A planned longitudinal study specifically designed to address the hypotheses would prove more statistically and contextually robust. The methodologies used by ALSPAC were based on the ELSPAC study and have evolved throughout the years as research techniques and technologies have improved. Originally, questionnaires and surveys were posted to respondents to complete and post back, while the current methodology for this type of data collection is via web portal (University of Bristol, 2020d), which involves less time and effort. Longitudinal attrition is a problem in any study and while the results presented here were of sufficient sample power, less attrition would have meant a more complete understanding of the thesis question in this population. Members of the child cohort are always welcome to 'rejoin the fold' and return to the project, regardless of how much time may have passed since they left (University of Bristol, 2020e). While the ALSPAC cohorts are accepted as a representational sample of the UK population for the purposes of generalising results (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001), there the

chronological cultural differences between this data and contemporary data might preclude generalising to the present-day population.

Several analyses in this work relied on data about the child cohort provided by the mother/primary caretaker. This is a non-issue for certain variables, i.e., a child may be incapable of describing their thoughts, feelings, and general cognition concerning a recent trauma at age 18 months but becomes more problematic as the child develops. Parents are able to report on child behaviour and that of the child's inner world they chose to share with their parents but may be reporting what they assume to be true or attribute based on that behaviour and not on its intentions. Thus, at a certain point, child-based data becomes approximations of the child's thoughts, feelings, and cognition. A longitudinal study designed to test the main hypothesis here could begin with parent-report data at birth, pair that with child-report data in middle childhood, and progress to purely child-report data throughout adolescence. Data selection during the design process would focus more on identifying and collecting contributory covariate data from the maternal childhood environment to the prenatal maternal environment, and from the early and middle childhood environments through adolescence. Socialisation and psychopathology would be measured with reliable, validated measures for use in a longitudinal design to ensure data consistency through the life of the study. A reliability index was provided when this statistic could be calculated, however for many of the scales used, only the sub-score, aggregate, or total score was sourced from ALSPAC.

ALSPAC is considered representative of the greater UK population but it is important to reiterate that the population cohorts had a high degree of racial homogeneity. This was acknowledged as a limitation of the study, as only 2.2% of ALSPAC mothers were non-white, compared to 4.1% in the Avon catchment area and 7.6% in the Great Britain population (Fraser et al., 2012), and 96.09% of the ALSPAC child cohort was white, compared to a national sample of 86.5% (Boyd et al., 2012). While this is immaterial on an epigenetic level, as there is no evidence for differences in epigenetic mechanism by race, cultural variables comprising one of the nested environments of both mother and child do vary in terms of race. It is hypothesised that similar results would be found in an equally homogeneous

majority non-white population or a racially mixed population after controlling for societally driven differences in several important variables known to vary by race.

While previously discussed, it bears reiteration here that the data used in establishing a model of the prenatal maternal social environment was gathered before the advent and common use of contemporary social media. Though human brain physiology evolves at a glacial pace, human culture does not, and social media has definitively changed interpersonal socialisation over the past few decades (Sadat, Ahmed, & Mohiuddin, 2014). Thus, it is possible that the results here represent a generational effect and contemporary social media socialisation may affect that effect. Listed here as a limitation, it is more a caveat to future research and replication attempts, and rather than controlling for social media use, it should be embraced as part of the study design. The hypotheses tested here conceptualised socialisation on a primitive basis as threat and survival drive were central to the epigenetic processes being investigated, however, utilising modern data including social media socialisation could result in a model demonstrating the change in socialisation in the past few decades.

Finally, and most importantly, this project could be thought of in terms of latent results; observed data was used to uncover the unobserved effect of the hypothesis. The scale used to model the prenatal maternal social environment approximated the dimensions from the 13 items used but was not specifically designed to test dimensional models of socialisation just as the prenatal maternal socialisation profiles were not representative of actual groups, they were simply latent classifications based on factor scores. While the SDQ is a reliable measure for predicting psychopathology (Achenbach et al., 2008; Stringaris & Goodman, 2013), the trajectories derived from scores over 3 time points are statistical approximations of distress, a proxy measure used here for psychopathology. Categorisations made here represented statistical likelihood of outcomes and while individuals' scores may have indicated high levels of expressed distress, it remains unknown how they experienced or quantified that distress. Based on the representational nature of these findings, the results presented here cannot be conclusively attributed to specific epigenetic modifications without viewing the genomic or methylation data. While ALSPAC did collect such data for both mother and child during medical clinics,

research use has dwindled the supply and it is now only available at great need (Boyd et al., 2012; Fraser et al., 2013).

8.9. Conclusions

This work began with the observation that every human being is the product of every environment that preceded them. They are also, as has been demonstrated, the product of every environment they interact with. The constant drive for survival, to live and reproduce against all odds, also drove adaptation to each new environment and that propensity is evident in modern humans. While adaptation is not exclusive to humanity, through it the species has seen incredible success and come to a point where physical environmental adaptation is no longer a matter of survival. Despite this, the mechanisms of adaptation remain in motion, from a child *in utero* during famine to the countless changes occurring in the genome of any given individual over the course of their lives. Evolutionary adaptations grind on at a glacial pace while epigenetic adaptations are able to affect change within a lifespan, though as was evident here, those modifications may become maladaptive when the environment outstrips epigenetics.

The clinical implications of these results are promising, specifically as they challenge extant conceptualisations of personality and psychopathology. It is well accepted that the introversion/extraversion continuum is linked to CNS arousal (Fischer, Wik, & Fredrickson, 1997; Matthews & Gilliland, 1999) and that these physiological mechanisms can be influenced by prenatal factors (Welberg & Secki, 2008; Gao, Huang, & Li, 2016). The results here propose an environmental component to personality theory, that an individual may trend towards ‘introverted’ or ‘extraverted’ behaviour in part because this behaviour would be advantageous in a specific environment anticipated by their genome. Further, these findings encourage understanding psychopathologic behaviour from a survival-based point of view and a clinician could consider, “What about this individual’s environment is distressing and provoking reactive behaviour? What steps can be taken to help this individual change their environment or to disengage maladaptive behaviour and learn adaptive behaviour?”

The applications of the thesis hypothesis are not limited to clinical understanding of individual behaviour, but also the individual themselves. David Rosenhan's seminal paper 'On being sane in insane places' (Rosenhan, 1973) described the contextualisation of behaviour as symptomatic simply because an individual had been categorised as mentally ill and/or placed in a treatment facility. Concerns over the clinical dehumanisation of individuals diagnosed with mental illness was a central theme of this piece, which is mirrored in the contemporary controversy of over-prescription of antidepressants, anxiolytics, and other psychotropic medications (Ilyas & Moncrieff, 2012; Reid, 2013; Spence, 2013). Conceptualising mental illness and its symptomology as the consequence of previous environments and a reaction to current environments, particularly in relation to socialisation supports the biopsychosocial model of mental illness, suggesting modes of treatment that centre on the individual as a person, rather than the sufferer of a disease. While 'professionalised stigma' has been long acknowledged (Schulze & Angermeyer, 2003; Rao, Mahadevappa, Pillay, Sessay, Abraham, & Luty, 2009) and while initiatives aimed at reducing stigma have shown positive results (Schulze, 2007), it remains an issue (Horsfall, Cleary, & Hunt, 2010). Viewing a service user as an individual standing at the convergence of influential and contributory factors to psychopathology risk and understanding the impact of those environmental, socioeconomic, and psychosocial factors could grant both greater clinical awareness and empathy.

Viewing features of psychopathology as they relate to socialisation and survival could lead to new understandings of the experience of mental illness, especially where symptomology negatively affects socialisation. Psychosis is often considered "*the archetypal mental illness*" (Cooke & Kinderman, 2018) as it remains fixed in the popular subconscious as the representative ideal of insanity, but as discussed above, symptomology can be considered uncontrollable survival drive. Anxiety disorders feature hypervigilance, fear, and excessive worry (World Health Organization, 1992), which are all valuable survival traits in an unfamiliar or harsh environment. Depressive disorders are characterised by sadness and despair, but also by lack of energy, motivation, and pleasure as well as social withdrawal (World Health Organisation, 1992). An animal that is injured or unwell hides so it is less

vulnerable while weakened; depressive symptomology could promote survival by mimicking the 'hide and heal' instinct. These and other psychopathologies all affect individual socialisation and social behaviour, frequently negatively (Goodyer, Herbert, Tamplin, Secher, & Pearson, 1997; Kelly et al., 2011) at a time when social support is most critical (Corrigan & Phelan, 2004; Mueller, Nordt, Lauber, Rueesch, Meyer, & Roessler). Programs of supported socialisation have shown to be beneficial (Davidson, Haglund, Stayner, Rakfeldt, & Chinman, & Tebes, 2001; Davidson, Shahar, Stayner, Chinman, Rakfeldt, & Tebes, 2004), indicating that clinical intervention could assist those to whom increased socialisation would help, even if they have no social support of their own.

Reconceptualising the relationship between socialisation and psychopathology for intervention and treatment could result in new treatment initiatives benefiting individuals who are unable to socialise. Though the ALSPAC data used here predated the prevalence and popularity of social media, this new mode of socialising is unavoidable in the contemporary developed world. The body of research surrounding social media and the individual is divided, with some studies highlighting an increase in loneliness (Pittman & Reich, 2016), depression (Lin et al., 2016) and negative self-appraisal (Vogel, Rose, Roberts, & Eckles, 2014; Woods & Scott, 2016), and others noting it can help ease adjustment (DeAndrea, Ellison, LaRose, Steinfield, & Fiore, 2012), foster wellbeing via social support (Nabi, Prestin, & So, 2013; Best, Manktelow, & Taylor, 2014), and facilitating socialisation for 'introverts' who may have difficulty socialising in person (Amichai-Hamburger, Wainapel, & Fox, 2002; Spradlin, Cuttler, Bunce, & Carrier, 2019). Using Internet-based social media for pilot programs focused on mental health and wellbeing have shown early benefits in terms of individual support (Stawarz, Preist, & Coyle, 2019), availability (Naslund, Aschbrenner, Marsch, & Bartels, 2016), and personal improvement (Brijnath, Protheroe, Mahtani, & Antonaides, 2016). Smart phone apps focusing on improving mental health, changing problematic behaviour, and alleviating distress have also become plentiful on all major mobile platforms (McKay, Wright, Shill, Stephens, & Uccellini, 2019). Digital interventions could be critical in future understanding the relationships of socialisation, social phenotype, and experience of psychopathology.

This work has wider social implications as well. Though the general population has become more aware of the detrimental effects of loneliness and isolation on individual health and wellbeing (Morin, 2018; Valencia, 2020), evidence has shown that loneliness is at 'epidemic' rates in the contemporary world (Holt-Lundstad, 2017; Cacioppo & Cacioppo, 2018; Jeste, Lee, & Cacioppo, 2020). An understanding that both women and their unborn children are at risk from prenatal social isolation could inform policy at the health service level in the form of risk screening and clinical interventions, and on the community level with health initiates like prenatal social clubs. The findings here covering the psychosocial and socioeconomic predictors of prenatal social isolation could also form the basis of local government initiatives to address societal issues which contribute to social isolation for all individuals, not just expectant mothers. Finally, an awareness of the environmental contribution to overall psychopathology risk and psychopathology symptomology could also affect societal stigma surrounding mental illness. While stigmatisation of individuals experiencing psychopathology has markedly improved over the past century (Rössler, 2016), some negative perceptions remain (Seeman, Tang, Brown, & Ing, 2016).

The stated goal of the Avon Longitudinal Study of Parents and Children was to explore the interplay between the environment and the personal genome as both affect health outcomes (Golding, Pembrey, Jones, & the ALSPAC Study Team, 2001). The goal of this work was to examine the effect of a specific environment on mental health outcomes with the personal genome as the proposed mechanism of those outcomes. It was evident that, independent from other major influences, the prenatal maternal social environment had a specific effect on the trajectory of psychopathology in middle childhood, as affected by the child social environment. This effect was described statistically as risk and likelihood, suggesting no predestination, but acknowledging that individuals existing in an environment contra to their expected environment experienced mores distress than those enjoying their expected environment. It is hoped that in the years since data collection, that distress has eased.

The members of the ALSPAC child cohort have become adults and many are parents with children enrolled in the second generation of the study, who may in turn

enrol their potential future children. One day, their descendants may reflect back on the environments they were heir to, possibly in a time when complete understanding of behavioural epigenetics is a reality. This future would hopefully see socioeconomic inequality and discrimination alleviated, with trauma and psychopathology addressed and treated by a compassionate and understanding society. That a time might come where the hostile environments of social isolation are uncommon and the distress of maladaptive behaviour nearly unknown, would be one of the greatest triumphs of the species.

8.10. Chapter References

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Appendix A. Inventory of all maternal questionnaires/surveys

Maternal self-completed:

8 weeks gest.	'Your Environment' & 'Your Home and Lifestyle'
12 weeks gest.	'Having a Baby'
18 weeks gest.	'Your Pregnancy'
32 weeks gest.	'About Yourself'
8 weeks	'Me and My Baby'
8 months	'Looking After the Baby'
21 months	'Caring for a Toddler'
33 months	'Your Health, Events, and Feelings'
47 months	'Mother's New Questionnaire'
5 years, 1 month	'Study Mother's Questionnaire'
6 years, 1 month	'Mother's Lifestyle'
7 years, 1 month	'Mother and Home'
8 years, 1 month	'Mother and Family'
9 years, 2 months	'Mother of a 9 Year Old'
10 years, 2 months	'You and Your Surroundings'
11 years, 2 months	'Lifestyle and Health of Mother'
12 years, 1 month	'Twelve Years On'
2004	'You and Your Life'
2010	'You and Your Study Person Aged 19+'

Maternal completed, child-based:

4 weeks	'My Young Baby Boy/Girl'
6 months	'My Daughter/Son'
15 months	'My Infant Daughter/Son'
18 months	'Girl/Boy Toddler'
24 months	'My Little Boy/Girl'
30 months	'My Little Study Daughter/Son'
38 months	'My 3 Year Old Boy/Girl'

42 months	‘My Son’s/Daughter’s Health & Behaviour’
4 years, 6 months	‘My Young 4 Year Old Boy/Girl’
4 years, 9 months	‘Development & Health of my Son/Daughter’
5 years, 6 months	‘My 5 Year Old Son/Daughter’
5 years, 9 months	‘My School Boy/Girl’
6 years, 6 months	‘My Daughter/Son Growing Up’
6 years, 9 months	‘My Son/Daughter at School’
7 years, 6 months	‘My Son’s/Daughter’s Well-Being’
8 years, 1 month	‘Growing and Changing’
8 years, 6 months	‘My Son’s/Daughter’s Health’
8 years, 6 months	‘My Son/Daughter at Home & at School’
9 years	‘Your Son/Daughter at 9’
9 years, 7 months	‘Growing and Changing 2’
10 years	‘Girl/Boy Health and Happiness’
10 years, 8 months	‘Growing and Changing 3’
11 years	‘Being a Girl/Boy’
11 years, 8 months	‘Growing and Changing 4’
13 years	‘My Teenage Son/Daughter’
13 years	‘Wellbeing of my Teenage Son/Daughter’
13 years, 1 month	‘Growing and Changing 5’
14 years, 7 months	‘Growing and Changing 6’
15 years, 6 months	‘Growing and Changing 7’
16 years	‘Growing and Changing 8’
16 years	‘Your Daughter/Son 16+Years On’
16 years	‘Year 11 Questionnaire for Parents and Carers’
17 years	‘Growing and Changing 9’

Appendix B. Inventory of all child-completed questionnaires

5 years, 6 months	‘Your Own Questionnaire’
5 years, 9 months	‘My Second Questionnaire’
6 years	‘Your Next Questionnaire’
6 years, 6 months	‘Growing Up’
6 years, 9 months	‘My Questionnaire’
7 years	‘Things for You to Do’
7 years, 6 months	‘My Teeth’
8 years	‘Me and My School’
8 years, 6 months	‘Some More About Me’
9 years, 2 months	‘My World’
9 years, 8 months	‘My Hands, My Feet, and Me’
10 years, 2 months	‘Rings & Things’
10 years, 8 months	‘Teeth and Things’
11 years	‘School Life and Me’
11 years	‘Watches and Funny Feelings’
12 years	‘All Around Me’
13 years	‘Food and Things’
13 years	‘Reading and Singing’
13 years	‘Travelling, Leisure, and School’
13 years	‘Experiences, Thoughts, and Behaviour’
14 years	‘Life of a Teenager’
15 years, 6 months	‘You and Your Friends’
16 years	‘Life of a 16+ Teenager’
16 years	‘Year 11 Questionnaire for Young People’
17 years, 6 months	‘DCSF Online Survey’
18 years	‘Your Changing Life’
18 years	‘Internet Use’
18 years	‘Gambling’
19 years, 6 months	‘You and Your Body’
20+ years	‘It’s All About You 20+’
21+ years	‘Your Life Now’

22+ years	‘Life at 22+’
23+ years	‘Life at 23+’

Appendix C. Data User Responsibilities Agreement

University of BRISTOL

ALSPAC
Bristol Medical School
Oakfield House, Oakfield Grove
Bristol, BS8 2BN

www.alspac.bristol.ac.uk

ALSPAC Data User Responsibilities Agreement

Please complete **all** the following boxes:

Name:	Amanda Spilkol	Institution:	Ulster University
Email:	spilkol-a@ulster.ac.uk		
B number:	B3395	Date project approved:	03/04/2019
Project title:	Offspring adaptation to social isolation: Testing a novel prenatal social environment adaptation hypothesis		
Project end date:	30/09/2020	Role within project:	Researcher
Institutional information security policy link:	https://www.ulster.ac.uk/__data/assets/pdf_file/0006/335796/EIA-and-ISMS-Policy.pdf		

The information obtained by ALSPAC has been given by the study participants on the understanding that it will be treated confidentially and anonymously. The ALSPAC Access Policy, available on the ALSPAC website, provides more detail and is referred to in the following agreement. For each point below please delete as appropriate **(note that NA means 'Not Applicable')** and sign the form to indicate that you will abide by the following:

1. I will not share my dataset with anyone, including other researchers except those named on the proposal form and approved by the ALSPAC executive for this particular project. — Yes
2. I will only use my dataset for the approved purpose covered by the ALSPAC project B number above. I will submit an amendment if I wish to extend the scope of the project. I will not attempt to match my dataset with any other that may have been provided by ALSPAC for previous projects. — Yes
3. I will not try to identify any study participants. I will notify ALSPAC immediately if I inadvertently identify an individual and I will not attempt to contact that individual. — Yes
4. If my project involves potentially identifying data, I understand that the data will only be released using ALSPAC's split stage protocol. I confirm I have read and understand the procedures for this process stated in the Access Policy (see Appendix Three). — Yes
5. Prior to submission of any papers for publication, I will complete a papers checklist and submit it, along with the manuscript to the ALSPAC executive for approval. I will do this at least two weeks prior to journal submission. — Yes
6. I will securely destroy any ALSPAC datasets when my approved project ends. — Yes
7. I understand that the University of Bristol owns the ALSPAC resource and any derivations from it (see Appendix Five of the Access Policy). Prior to destruction I will return my dataset to ALSPAC, together with the scripts/syntax and relevant documentation required to generate derivations. The documentation will be sufficient for someone else to understand and replicate my analyses. — Yes
8. If my dataset contains data from linked third party records, I will comply with any additional instructions as provided by ALSPAC. — Yes

9. I will adhere to relevant data protection legislation, including the EU General Data Protection Regulation (https://www.eugdpr.org/) and UK Data Protection Bill 2018	Yes
10. I will notify ALSPAC in advance, if not already agreed, when any datasets are required to be transferred across any country's borders that are not within the European Economic Area (EEA)	Yes
11. I have read Appendix Four in the Access Policy regarding 'Information security controls' and will comply. Please note the requirements that that all hardware storage must be encrypted and kept with you at all times or be in a securely locked location.	Yes
12. I understand that ALSPAC will maintain a record of my contact details in order to contact me about my use of the data.	Yes
13. I consent to ALSPAC using my contact details in order to provide ongoing news about the ALSPAC research study in the future.	Yes
14. I will promptly notify ALSPAC (alsp-infosec@bristol.ac.uk) about any breach of ALSPAC data or incident that may have compromised the security (i.e. confidentiality, integrity or availability) of the ALSPAC data.	Yes

Signature: ..... **Date:** 20/05/2019

Your use of ALSPAC data is controlled by the terms of a legally binding contract [or your University of Bristol contract of employment if you are a UoB employee]. Failure to abide by the above rules could result in exclusion of your institution (or yourself if you are a UoB employee) from further access to ALSPAC data and you will be subject to all appropriate sanctions, where applicable.

Please return your completed form to your assigned data buddy

The ALSPAC privacy notice is available at http://www.bristol.ac.uk/alspac/participants/privacy/

Appendix D. Life events inventory (42 items)

Taken from: Bishop, J., Herrick, D., Stowe, B., Golding, J., and the ALSPAC Study Team. (2008). *Data collected from the questionnaires 'Having a Baby' & 'Home and Lifestyle'*. Unpublished manuscript, University of Bristol, Bristol, UK.)

Since becoming pregnant:

1. Your partner died.
2. One of your children died.
3. A friend or relative died.
4. One of your children was ill.
5. Your partner was ill.
6. A friend or relative was ill.
7. You were admitted to hospital.
8. You were in trouble with the law.
9. You were divorced.
10. You found that your partner didn't want your child.
11. You were very ill.
12. Your partner lost his job.
13. Your partner had problems at work.
14. You had problems at work.
15. You lost your job.
16. Your partner went away.
17. Your partner was in trouble with the law.
18. You and your partner separated.
19. Your income was reduced.
20. You argued with your partner.
21. You had arguments with your friends or family.
22. You moved house.
23. Your partner hurt you physically.
24. You became homeless.
25. You had a major financial problem.
26. You got married.

27. Your partner hurt your children physically.
28. You attempted suicide.
29. You were convicted of an offence.
30. You were bleeding and thought you might miscarry.
31. You started a new job.
32. You had a test to see if your baby was abnormal.
33. You had a result on a test that suggested your baby might not be normal.
34. You were told you were going to have twins.
35. You heard that something that happened might be harmful to the baby.
36. You tried to have an abortion.
37. You took an examination.
38. Your partner was emotionally cruel to you.
39. Your partner was emotionally cruel to your children.
40. Your house or car was burgled.
41. You had an accident.
42. a) Is there anything else which is not on the list which has concerned you or required additional effort from you to cope since becoming pregnant?
    b) If yes, please describe: How did this effect you?
    c) 1 – a lot, 2 – moderately, 3 – mildly, 4 – not at all